Theo Ritchie

GYNECOLOGICAL AND OBSTETRICAL PATHOLOGY

GYNECOLOGICAL AND OBSTETRICAL PATHOLOGY

INCLUDING CHAPTERS ON THE NORMAL HISTOLOGY AND THE PHYSIOLOGY OF THE FEMALE GENITAL TRACT

BY

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WITH 338 ILLUSTRATIONS, OF WHICH 281 WERE DRAWN BY THE AUTHOR

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PREFACE

In this volume I have attempted to co-relate information of interest to the clinician and pathologist in such a fashion that both will derive full benefit from this conjunction. Many books are written solely from the viewpoint of clinical medicine, others from the laboratory standpoint alone. Full efficiency can be attained only by combining the two.

The general pathologist, and his number is increasing, as standardization spreads and grows, requires a reference book containing not only illustrations of pathological conditions but also an atlas of normal histology. He should welcome a book which contains facts vital for correct diagnosis, reference to the original sources from which they are gathered, and interpretations in terms of clinical significance. Nor can the clinician dispense with these aids to diagnosis and rational therapy.

In foreign books the American and English literature has been consistently slighted. I have tried to do justice to Anglo-Saxon publications, by no means an easy task, considering the widely scattered material and the huge number of periodicals requiring consideration. To save space, much information has been placed among the literature in the form of compressed addenda.

The illustrations, with the exceptions specifically mentioned (that is, photomicrographs and a very few drawings taken from other sources), were drawn by me from my collection of specimens.

As illustrations of gross specimens are readily found in almost all textbooks on gynecology, I reduced their number to a minimum and thus was able to increase the number of pictures of microscopic sections. I owe thanks to many colleagues for their aid in obtaining specimens of uncommon conditions. Among those to whom thanks are specially due are Dr. J. Brettauer, Professor F. C. Wood, Drs. Eli Moschcowitz and F. S. Mandlebaum.

Controversial matter, which has so often frightened away would-be students of pathology, has been reduced to a minimum. Theory, too, has not been featured. On the other hand, facts have been gathered, arranged and simplified so as to make them readily available and useful.

The microscopical sections are classified as magnified to *Very Low Power,* × 18 to × 26; *Low Power,* × 70 to × 105; *Medium Power,* × 210 to × 325; and *High Power,* × 400 to × 600.

In addition to the monographic literature the following authorities have been freely consulted: VEIT, Handbuch der Gynäkologie (2d ed.); EDEN AND LOCKYER, New System of Gynecology; v. WINCKEL, Handbuch der Geburtshilfe; WINTER, Gynäkologische Diagnostic; KELLY, Operative Gynecology (1st and 2d eds.); WILLIAMS, Obstetrics (4th ed.); KELLY AND CULLEN, Myomata of the Uterus; CULLEN, Cancer of the Uterus; GEBHARD, and also FRANKL, Pathologische Anatomie der weiblichen Sexualorgane; KAUFMANN, Spezielle Pathologische Anatomie; EWING, Neoplastic Diseases; NORRIS, Gonorrhea in Women; the Anatomies of HENLE, QUAIN, CUNNINGHAM, PIERSOL, POIRIER AND CHARPY, etc.

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DENVER, COLO.

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CHAPTER I

INTRODUCTORY

Coöperation between the clinician and the pathologist is necessary in order to obtain the most useful results. The pathologist ought not to be a stranger at the bedside or in the operating room. The clinician should prove a welcome guest in the laboratory or at the autopsy table.

Frequently these intimate relations do not exist. The pathologist remains isolated in his laboratory, receives innumerable jars and bottles containing specimens, and without volition allows himself to become immersed in the purely theoretical phase of his subject.

The clinician on the other hand may visit the laboratory once or twice each year, with the object of seeing during the course of one short hour, all the material he is interested in.

This opening chapter deals with the ways and means of attaining proper and sympathetic relations.

The clinician should supply an outline of the history of the case, a description of from where and how the material is obtained, and a note of the particular information which is of immediate interest to him. He should also deliver the material *at once,* if it is to be handed over in the fresh state, or put it up in the proper fixative if occasion demands this.

I. **History.**—The history must begin with the age of the patient. The age is of great importance. A much thickened endometrium, for instance, might be quite normal in a young woman just before her menstrual period, but on the other hand, in an old woman, long past the menopause, it might signify malignancy.

The duration of the disease often gives valuable information. A tumor in the posterior sheath of the rectus muscle which has not increased in size for many years, may prove to be a typical desmoid fibro-sarcoma with no tendency to recurrence. A similar tumor, histologically identical, if of rapid growth might be excessively malignant, or a growth, morphologically identical might be due to inflammatory reaction if a laparotomy had been performed some time previously.

The derivation of a specimen is also of utmost importance. Adenomatous tumors may serve as example. Adenomata of the intestine or of the breast are usually benign. In the uterus, however, adenomata of the mucosa are always malignant, eventually to be classed with adenocarcinomata. If only tumor material is removed, and no surrounding healthy tissue supplied, the pathologist is left at sea.

Frequently a *particular region* in the specimen is of special interest to the clinician. It may be an outlying portion of the parametrium in a complete hysterectomy for cancer. The operator is then anxious to know whether the infiltrated area consists of carcinomatous or inflammatory tissue. He should, therefore, mark this region plainly, and specifically demand a report upon this particular point. If, for instance, an ectopic pregnancy occurs in the stump of a previously excised tube, the operator will want to know whether the tubal remnant was patent or not. Let him ask for this information.

Additional information attached to the request for examination may often prove of great service to the pathologist. To illustrate this the following case may be instanced:

After vaginal hysterectomy a polypoid bleeding growth is noted in the fornix. The primary operation was performed for carcinoma of the body of the uterus and, therefore, the bleeding growth causes anxiety. It may, however, be due to a prolapse of the fallopian tube. A hint to this effect might prevent serious error, as sections from such an inflamed and displaced tube are not unlike a recurrence from an adenoma malignum.

The pathologist on the other hand should be ready to attend operations in order to prepare frozen sections at once, should the occasion require it. He should be familiar with the gross appearance of lesions, and be able to advise upon the immediate course to be pursued. Every operator of experience realizes that valuable specimens are irretrievably ruined or lost because during the press of the operation, the opening of the specimen may have to be entrusted to a recent interne or even to the casual spectator.

II. **The Pathological Report.**—A report to be of real value should contain the following information:

1. The gross description.
2. The histology.
3. The diagnosis $\begin{cases} \text{certain.} \\ \text{uncertain.} \end{cases}$
4. The prognosis from the pathological viewpoint.
5. Therapeutic advice, if indicated.
6. The casuistic or theoretical interest of the condition in special instances.

1. The Gross Description should be concise and clear. It is of special importance if the specimen has not been cut open in the operating room. Careful dissection in the laboratory may then reveal information of

utmost value. In involved inflammatory conditions such examination may show that part of the ovary has been left behind. This will prevent surprise when the menses reappear, and reports of menstruation after removal of the ovaries will then disappear from literature. Study of an intraligamentous tumor may show a piece of the ureter attached to the growth, thus calling the attention of the surgeon to a serious accident, etc.

2. The Histology.—As a rule a few words will suffice. Often the diagnosis will include the histology. "Squamous celled carcinoma of the cervix uteri" may sufficiently describe a given specimen. "Pseudomyxomatous ovarian cyst" may convey enough information concerning another.

Occasion may arise when additional information should be given. "Sarcomatous changes in a uterine fibroid" for example might unduly alarm the operator. If qualified by the statement that "in the center of the large fibroid tumor only a small area shows sarcomatous degeneration" the report would be more reassuring. A report of "solid alveolar carcinoma of the uterine body," after hysterectomy, means less than if the pathologist adds—"from the type of distribution of these cells it appears that the growth is metastatic. The single ovary and tube attached to the specimen are normal. Either the adnexa which were not removed, or some other primary focus must be sought for."

3. Diagnosis.—In most instances the histology will include the diagnosis. In the case of tumors the classification is usually sufficiently descriptive to include both. The same applies to such inflammatory conditions, as bartholinian abscess, chronic metritis, tubercular salpingitis, corpus luteum abscess, etc. Frequently multiple associated lesions are unexpectedly encountered. Sometimes the changes do not correspond to the usual type. Under these and similar circumstances the histopathology should be carefully described.

Most unsatisfactory is the report which must be qualified because no certain or definite diagnosis can be made.

A uterine polyp may show signs suspicious of sarcomatous degeneration, but not sufficiently so to warrant the advice to perform hysterectomy; or the base of the polyp may not have been included in the specimen, in which case it may prove impossible to make a diagnosis. Curettings may resemble chorionepithelioma, but as no muscle tissue was contained in the material, it may not be feasible to determine or exclude invasive tendencies. Sometimes a specimen may prove too necrotic to permit of accurate histological examination.

Under these and similar circumstances the pathologist must admit his limitations. He should call the clinician's attention to the difficulties encountered, seek to coöperate heartily, and share the burden of the ultimate decision. It may also happen that the sections look as if a malignant process were just beginning (as in excisions from early carcinoma of the cervix) or that slides from a fibroid show what the Germans term "an appearance of unrest." Here, experience and judgment are of utmost value. It may be wise to request more material

from the same source, to counsel further and prolonged observation of the patient, or to consult and compare notes with other pathologists in very special instances.

4. Prognosis.—Wherever possible some attempt to indicate the prognosis is called for. In tumors to which this especially applies, a prognosis based solely upon the histology of the growth is rarely of value. When this, however, can be reinforced by deductions founded upon other facts, valuable hints may be given. For instance a scirrhus cancer of the breast in an old woman is rarely hypermalignant. In another case only one ovary has been removed, and adenocarcinoma diagnosed in the ablated organ. The pathologist might well draw the clinician's attention to the fact that recurrence in the other ovary is the rule, in 90 per cent. Certain types of ovarian sarcoma recur almost without exception. This should be mentioned. So-called Krukenberg tumors of the ovary are never primary. The clinician should be cautioned to look for a primary growth in the stomach and intestine, uterus and breast. These examples can be multiplied indefinitely.

5. Therapeutic Indications.—Not infrequently therapeutic advice must be volunteered. If a supravaginally amputated fibroid uterus shows sarcomatous changes at the line of amputation, the operator must be advised to remove the cervix at once. Or a uterine carcinoma may, on examination be found to extend microscopically to the edge of the vaginal cuff. The operator, when told of this, may still be able to excise more vagina. The importance of such hints as those just suggested will, of course, depend largely upon the experience of the clinician. Nevertheless no physician will object to such suggestions if they are conveyed judiciously and in the proper manner.

6. Theoretical Considerations.—Occasionally a specimen may prove to be unusually rare or of special importance. If the clinician's interest is aroused, he will study the condition and put it on record. Unless this is done, many valuable observations are lost to the literature.

So far we have chiefly spoken of specimens excised for diagnosis, curettings and operatively removed organs. Similar methods apply to autopsy material as well.

III. **Autopsy.**—Whenever a complete autopsy has been granted, the pathologist will, of course, perform the post mortem examination as thoroughly as possible. He will make note of all deviations from the normal. The clinician, however, desires information which bears upon the chief symptoms noted during the last illness. The pathologist should make every effort to assist. He may have to deviate from his routine method of procedure, but should submit to this inconvenience readily and cheerfully. In a case of puerperal infection a long and tedious dissection of the pelvic lymph channels may be necessary. A death from internal hemorrhage after operation may require injection of colored fluid through the veins and arteries in order to determine the

bleeding point. Unless this special effort is made, autopsies lose their value and importance to the clinician.

The foregoing has been offered as a hint and an outline of the ways and means to encourage cordial relations between the practitioner and pathologist. The experienced gynecologist will know many of the facts referred to; the "gynecological pathologist" may consider most of them trite. The occasional "gynic" operator will derive benefit from them. The same applies to the general pathologist, to whom gynecological pathology is but a side issue.

CHAPTER II

TECHNIC

Only such methods as have proved their value in routine examinations will be discussed. Special technics are now readily accessible in many text books. Of these Malory and Wright, and Lee in English, and Schmorl in German, are particularly valuable (1).

1. FIXATION.—*Formalin* (Formaldehyde 35 to 40 per cent) is the most generally useful reagent. It should be used in strengths of 4 and 10 per cent. (To prepare 4 per cent formalin take 10 c.c. of formalin and add 90 c.c. of water; for a 10 per cent solution take respectively 25 and 75 c.c.). As the penetration of the reagent is rapid and deep, large blocks of tissue or entire specimens may be used. As soon as fixation is complete, in from 2 to 3 hours for thin pieces, to from 2 to 5 days for large specimens such as uteri, tumors, etc., depending on their size, change to 80 per cent alcohol for future preservation.[1]

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[1] Throughout this chapter average limits of time for fixation, hardening, embedding, and staining will be indicated. The time is relative and variable, but for the convenience of beginners, certain arbitrary limits must be imposed. With increasing personal experience, these may be adhered to less and less strictly.

The weaker solutions and longer periods are used where increased length of time is of little moment (as 4 per cent formalin instead of 10 per cent), and where finer histological details are desired. For as a rule, increased strength and penetrative power or higher temperatures can only be employed at the cost of increased distortion and loss of minute detail. Similarly a transfer of material from an aqueous solution to 80 per cent alcohol will entail more shrinkage than more gradual changes through 30 per cent, 50 and 80). In routine work it is unnecessary to observe such tedious and time-consuming refinements of technic.

The number of hours first mentioned will apply to *thin pieces* of from 2 to 4 mm. ($^1/_{16}$ to ⅛ in.), the second number to *thick pieces* of from 1 to 1.5 cm. (⅜ to ⅝ in.). The other dimensions (breadth and length) are of no moment except that it should be borne in mind that large sections are always more difficult to cut than small ones.

Formalin fixation is completed when the tissues are bleached to a grayish white (make equidistant parallel cuts to determine this). Orth's and Müller's fluid impart a yellow brown color through the entire depth of the specimen. With alcohol the blood in the specimens may appear brown. The tissue at the end of fixation should be firm, elastic but not brittle. The proper consistence may be compared to that obtained on palpating the cartilage of the nose. Fixation or hardening beyond this stage makes the tissues brittle and unfit for sectioning. Specimens, previously fixed, may be kept in 80 per cent alcohol for long periods without altering their consistence.

In fixation, hardening, and in fact, in all the procedures to be mentioned, the volume of fluid must exceed the volume of the specimen by at least five times. The fluid must have access to the tissues on all sides (cotton at bottom of jar). This applies especially to fixation.

Alcohol is to be used only if bacteria or glycogen are to be looked for. Fixation is obtained in 96 per cent concentration. The specimens are preserved in 80 to 90 per cent alcohol. The shrinkage produced by alcohol distorts finer histological details. Pieces thicker than 1 to 1.5 cm. are not to be employed.

Orth's Fluid combines some of the advantages of formalin and Müller's fluid. It is of use in fixing large masses of muscle and connective tissue (uterus), which in pure formalin rapidly become hard and brittle. Used for 24 hours.

$$\left.\begin{array}{l}\left.\begin{array}{ll}\text{Potassium Bichromate} & 2.5\\ \text{Sodium Sulphate.....} & 1.0\\ \text{Aqua Destillata......} & 100.0\end{array}\right\}= \textit{Müller's Fluid}......90.0\\ \qquad\qquad\qquad\qquad\qquad\qquad\text{Formalin 10\%......10.0}\end{array}\right\}= \textit{Orth's Fluid}$$

Müller's fluid, the composition of which was just indicated, fixes the uterus best of all. It requires weeks, however, to accomplish fixation and hardening (two weeks in the thermostat at 37°, or 4 to 5 weeks at room temperature). The reagent must be renewed at least after 48 hours and again after seven days (whenever the solution becomes cloudy). Either formalin or Orth's fluid, if allowed to act no more than the proper length of time, will suffice for ordinary demands.

Carnoy's Fluid is useful for very rapid fixation of small pieces.

Alcohol, absolute	6.
Glacial acetic acid	1.
Chloroform	3.

Fix for 1 to 3 hours, then absolute alcohol (two changes) 3 to 24 hours, embed.

2. Hardening and Dehydration in Ascending Alcohols.—Material fixed in formalin for 24 hours does not require preliminary washing unless there is much blood or pigment in the tissue. Tissues kept in formalin for long periods and therefore rendered hard and brittle can be restored by prolonged washing (24 to 48 hours) in running water. Tissues fixed in Orth's or Müller's fluid should always be thoroughly washed in running water for from 6 (pieces) to 24 hours (organs). The material when cut up for embedding is then transferred to 80 per cent alcohol for from 12 to 24 hours, next to 95 per cent alcohol for the same length of time, and finally to absolute alcohol for from 2 to 12 hours. Too long a stay in absolute alcohol again renders the tissues brittle.

3. Methods to Be Employed in Sectioning.

Frozen sections.
Cullen's method.
Celloidin method
Paraffin method.

Frozen sections are not only of value where immediate diagnosis is required, but can be employed with advantage for orientation, when many portions of a large specimen have to be examined. If any area proves of special interest or importance paraffin or celloidin sections of this region can then be made. In this way the time and labor involved in embedding will be saved.

Frozen sections are regularly employed when *glycogen* or *fat* are to be looked for.

Excellent service can be obtained from simple table microtomes as well as with the automatic lever models. Carbon dioxid cylinders furnish the most convenient freezing mixture, although the hand bulb ether apparatus will suffice where cylinders cannot be obtained. (Bardeen's CO_2 microtome.)

The material for frozen sections must be selected with care. Fresh tissues can be cut with ease if immediate diagnosis is desired. Better sections, are, however, obtained if very small and thin segments (1 by 1 cm., 3 mm. thick) are fixed in 10 per cent formalin for 30 minutes. The formalin should be removed by washing. Material preserved in alcohol must first be washed in water 12 to 24 hours. Otherwise it cannot be frozen.

Very fatty material, like glands embedded in axillary fat, if thin sections are required, must be passed through the ascending alcohols, the fat removed by immersions in ether, and the block again placed in water before cutting. Where small segments are used a few hours suffices for these added steps.

Cullen's method for the rapid cutting and staining of specimens for diagnosis is as follows (2):

1. Frozen section in 5 per cent formalin for 3 to 5 minutes.
2. 50 per cent alcohol 3 minutes.
3. Absolute alcohol 1 minute.
4. Wash in water.
5. Stain in hematoxylin 2 minutes.
6. Decolorize in acid alcohol.
7. Rinse in water.
8. Stain in eosin.
9. 95 per cent alcohol.
10. Absolute alcohol, oil of cloves or creosote, mount in balsam.

The Celloidin Method is particularly suited for those who do only occasional histological work. It requires few appliances and answers the ordinary requirements perfectly. Very large sections are more readily cut in celloidin than in paraffin.

The dehydrated block of tissue is placed in a mixture of equal parts of absolute alcohol and ether for from 12 to 48 hours. It is then left in thin celloidin (prepared by covering *dry* celloidin with alcohol until it has swollen, and then adding an equal quantity of ether to the mixture) for

24 hours or more. The tissue is now transferred to thick celloidin (syrupy consistence) for the same period. (The consistence of celloidin depends upon the amount of alcohol and ether (always $\overline{aa}$) added. Thin celloidin rapidly thickens if allowed to evaporate in a partly covered jar). The tissue is next placed upon the roughened surface of a wood or vulcanite block (or ribbed blocks may be purchased), covered with more celloidin which is repeatedly dripped over it, and allowed to harden under a bell jar for a few hours. The hardening can be hastened by putting a small open dish containing chloroform under the bell jar. Further hardening and also permanent preservation is obtained by storing in 80 per cent alcohol. Hardening is completed when the celloidin has attained the consistence of rubber used in erasers. Pieces of tissue up to two inches long and one-half inch thick can be cut without trouble.

Steps in Celloidin Embedding

1. Dehydration.
2. Alcohol absolute and ether equal parts of each for 12 hours.
3. Thin celloidin 24 hours to 5 days.
4. Thick celloidin 24 hours to 5 days.
5. Blocking, and hardening under bell jar 1 to 3 hours.
6. Final hardening and storing in 80 per cent alcohol.

The following is a rapid method of celloidin embedding for diagnostic work (Stepanow) (3).

1. Dehydrate by frequent changes in absolute alcohol.
2. Impregnate for 3 to 6 hours in the following mixture.

Celloidin	15 gm.
Oil of cloves	50 c.c.
Ether	200 c.c.
Absolute alcohol	10 c.c.

3. Block and harden in chloroform fumes.

Paraffin Method.—The writer has found this method the most useful. By means of it the thinnest and most perfect sections are obtained. Unstained sections (kept either between sheets of packing paper, or fixed on slides) can be preserved indefinitely. Blocks of uncut tissues can be stored for years, dry, in labeled boxes.

A thermostat regulated to maintain a temperature of 57° to 60° C. is necessary.

The dehydrated tissue is placed in chloroform for 1 to 2 hours. It is then transferred to a saturated solution of paraffin in chloroform 1 to 12 hours, which is, toward the end of this time, placed on the top of the thermostat.[2] The tissue is then dropped into fluid paraffin, and kept in the

[2] Chloroform paraffin is prepared by adding crumbs of waste paraffin to 2℥ of chloroform, kept warmed upon the top of the thermostat. When no more paraffin dissolves the bottle is cooled and excess paraffin crystallizes out. The clear fluid is used.

thermostat for 1 to 4 hours (*paraffin of 50° melting point* obtained by mixing 30 g. paraffin of 45° melting point with 25 g. of 56° paraffin). The

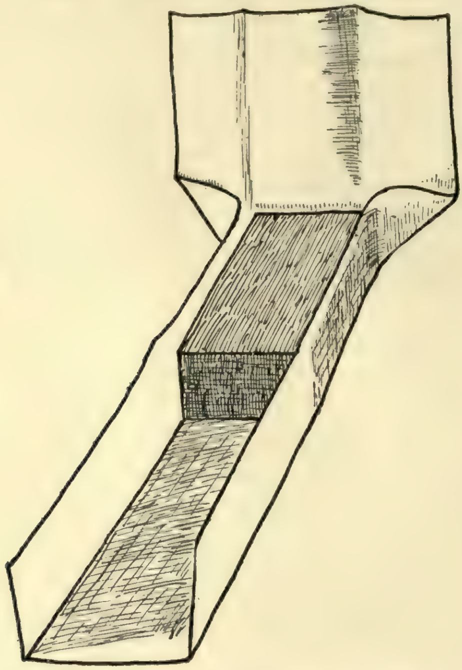

FIG. 1.—ACTONE: IN FOLDING PAPER TO FORM PARAFFIN TROUGH. A vulcanite block is used to give the proper shape and size.

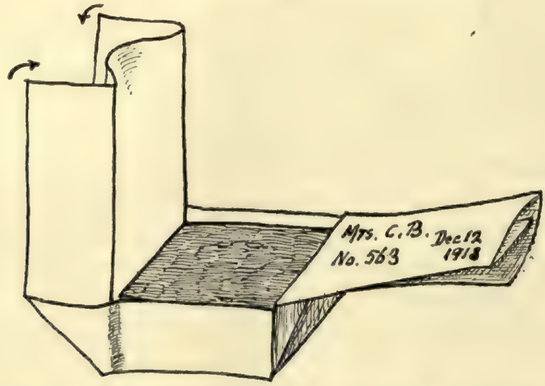

FIG. 2.—ACT TWO: PREPARATION OF PAPER PARAFFIN TROUGH. Right side completed; arrows on left show method of overlapping. Vulcanite block is squeezed out when trough is completed.

paraffin should be changed three times to remove all chloroform. The object is then arranged with a warm forceps in a paper trough (Figs. 1 and 2), into which a little melted paraffin has been poured, and fluid paraffin

carefully added until the trough is filled. As soon as a firm pellicle forms on the surface, the paper container is at once submerged in ice water until the entire block has hardened. Unless the cooling is sudden, paraffin hardens in crystalline form unsuitable for sectioning.

Steps in Paraffin Embedding

1. Dehydration.
2. Chloroform, 1 to 2 hours.
3. Chloroform paraffin, 1 to 2 hours.
4. Melted paraffin (50°), 1 to 4 hours; three changes.
5. Blocking and *rapid cooling.*

(Cedarwood oil replaces or acts as an adjuvant to chloroform if the tissues are brittle. The tissues are left in the oil until they are clear and translucent and then transferred directly to melted paraffin or left in chloroform before taking the usual steps.)

The following is a rapid paraffin method suitable for very small pieces of tissue:

1. Fresh tissues into absolute alcohol for 45 minutes (3 changes).
2. Acetone, 15 minutes.
3. Xylol, 30 minutes.
4. Paraffin, 30 minutes (3 changes).
5. Block and cool.

More rapid and more perfect imbibition with paraffin is obtained by using the *vacuum method,* which shortens the process to 15 to 30 minutes (Harvey, 4). In this method the bottle containing the tissue immersed in the warm paraffin is connected with a Sprengle's air pump by means of an air-tight system of stoppers and tubes. In order to guard against accidental backflow of water (if the faucet is shut off prematurely) a mercury trap is placed in the line.

4. Section Cutting.—*Frozen Sections.*—Small pieces of tissue (1 by 1 cm. by 3 mm. thick) (removed from formalin or water) are firmly pressed upon the freezing plate of the microtome. The carbon dioxid, or ether spray, is then set going until the tissue is hard. The hand knife wiped dry (to prevent the curling of sections) is moved rapidly forward and backward (with beveled edge facing downward) while the micrometer screw is simultaneously turned upward. If the tissue is frozen too hard a gritty sensation is experienced and the sections tear. Wait until the tissue grows less cold (breathe upon the surface). A large number of sections are rapidly cut, and allowed to accumulate upon the knife blade. They are removed by gently swishing the blade in a bowl of water, in which the sections are to be floated. The knife should be held at an angle of 35° to 45° to the surface of the microtome. Sections of from 5 to 15 micra may readily be cut.

Celloidin section cutting.—Any standard model of the sliding microtome, preferably one with automatic feed, will do. A Naple's clamp is required to hold the blocks to which the embedded tissues are fastened.

The celloidin is trimmed to within a few millimeters of the tissue. The block is adjusted so that the long diameter of the specimen is parallel to the long axis of the microtome. The knife is arranged to cut at such an angle that the first part of the cut is made by the heel, the last part by the tip of the microtome blade. A very slight tilt is of advantage. This is usually arranged for by the construction of the knife. The blade must be kept thoroughly moistened with 80 per cent alcohol, and each section, as soon as cut, is lifted from the knife by means of a camel's hair brush, and placed in a flat dish containing 80 per cent alcohol.

Sections of from 8 to 15 micra are readily obtained. To cut thinner sections, it is first necessary to cut until the tissue surface is perfectly smooth. The surface and the block are then dried, and a film of very thin celloidin applied. By blowing on this the film dries and hardens in an instant. The section, supported by the additional celloidin, is cut and the process repeated.

Paraffin Section Cutting.—The sliding microtome is quite serviceable in cutting single paraffin sections or short ribbon sections. The knife must be adjusted at a right angle, the longest diameter of the specimen being also at a right angle, to the slide of the microtome, and parallel to the knife edge. A Minot rotary paraffin microtome is to be preferred.

The embedded specimen is fastened to the plate specimen holder by means of heat (in case a Naple's clamp is used, to a wood block), the edges trimmed close to the tissue, and care taken to have opposite edges parallel.

The knife is used dry. If sections are brittle the knife should be slightly warmed; if the paraffin creases, the block must be cooled (ice box) or in winter time the window is opened. By cutting rapidly the edges of succeeding sections cohere and ribbons are formed. With the Minot model gravity causes the ribbon to move along; with the sliding model a light camel's hair brush is used to push the sections across the knife.

Individual sections or ribbons are transferred to a dish containing *boiled* water at about 50° C. The warmth flattens the sections and smooths out all wrinkles. A sufficient number of sections are floated upon slides previously cleaned with alcohol and ether, part of the water drained off by tilting, and the slides placed horizontally in or on the thermostat for 6 to 12 hours to dry. If capillary action does not fix the specimen firmly (chiefly when Müller's fluid has been used) *Mayer's albumen* (Mayer's albumen: Take 10 gms. white of egg, beat to a lather and filter through a plaited filter. This may take 24 hours. Add 10 c.c. pure glycerine and 0.2 gm. sodium salicylate dissolved in a teaspoonful of water. The albumen solution keeps indefinitely) may be employed as a fixative.

Sections of from 2 to 15 micra can be cut. In summer time paraffin

with a melting point of 56° is of advantage. Serial sections are almost always cut in paraffin. If a block is not used up it can be kept indefinitely.

5. STAINING AND MOUNTING.—*Frozen sections* from material previously fixed and hardened are treated exactly like celloidin sections. Those cut from fresh material are treated according to Cullen's method (p. 8). It may prove of advantage to catch the section on a clean slide, blot it firmly on to this with *dry* blotting paper, and perform the succeeding manipulations with the section adhering to the slide.

Celloidin sections are removed from 80 per cent alcohol by means of a spatula, and transferred to distilled water. Large numbers of sections can be expeditiously handled by putting them all into an ordinary fine-meshed tea-strainer which is dipped into the appropriate solutions.

Paraffin sections are ordinarily freed from the paraffin before staining. To accomplish this the slide to which the sections adhere is immersed in pure xylol (the process can be shortened by first slightly heating over a flame until the paraffin begins to melt) until the sections are clear. Transfer to absolute alcohol for one minute, to 95 per cent and 80 per cent alcohol for five minutes each, then place in water.

Hematoxylin and Eosin Staining. — Delafield's hematoxylin (well ripened), alcohol eosin, alcohols of 80 per cent, 95 per cent and absolute strength are required.

Sections prepared by any of the three methods are taken from distilled water and stained in *freshly filtered* hematoxylin for from one to five minutes. They should not be stained too darkly. Transfer to *tap* water until the blue tinge is evident (2 per cent lithium carbonate enhances the blue). Renew the tap water. Place in 80 per cent alcohol for five minutes. Transfer to the eosin for 30 to 60 seconds. Pass sections into 95 per cent alcohol for three minutes (and paraffin sections into absolute alcohol for one minute).

For particularly sharp differentiation overstain with hematoxylin, differentiate in acid alcohol until color is nearly gone, and neutralize with dilute ammonia (4 drops of ammonia to a tumbler of tap water). Then proceed as above.

Mounting.—Fresh or celloidin sections are put from 95 per cent alcohol into oil of origanum until entirely cleared. Paraffin sections are taken from absolute alcohol and placed in xylöl until cleared. The sections placed on or fixed to a slide are blotted, covered with balsam and protected by a cover glass. The slide is at once numbered and labeled.

For further details the reader is referred to text-books of histological methods and technic (l. c. 1).

Selection of Material.—CURETTINGS are spread on a glass plate; then suspicious pieces selected, and an effort made to choose material of varying appearance. If the curettings are scant the entire amount may be examined. Frozen sections of curettings rarely yield good slides. The celloidin or paraffin method should be preferred.

Specimens submitted for diagnosis are usually obtained from the vulva, vagina or cervix. Such specimens should always be examined (hand lens) for skin or mucous surfaces. Small pieces are cut entire, or small areas from large specimens removed for sectioning. Whenever possible the tissues should be trimmed so that the large flat surfaces are perpendicular to the skin or mucous membrane edge. This will facilitate orientation during embedding and cutting, and avoid artefacts due to slantingly cut epithelial borders. The edge opposite to the skin or mucosa should be trimmed straight, if possible, in order to facilitate identification.

Selection of Material from the Uterus.—If an entire uterus is submitted, pieces should be removed from different parts of the cervix and body, and cut so as to include the mucous membrane. Any suspicious areas are, of course, included in the selection. By cutting pieces of various shapes and sizes, and marking them on a diagram, future orientation is facilitated. Another method consists in fastening the pieces, after fixation, to labeled slips of paper by means of gum tragacanth (aqueous), and after a few minutes placing them in alcohol for dehydration. Projecting and polypoid growths are cut so as to include the adjoining uterine mucosa and musculature which form their base.

The routine method of opening the uterus is as follows:

The uterus should be split with a scalpel from cervix to fundus through either the anterior or posterior wall, laying open the endometrium. From the main line of incision two cuts, one to each tubal angle are then made. (Figs. 3 and 4.)

The Fallopian Tube is cut across transversely. Even small deviations will produce distortion and artefacts. It is best not to cut the tube until it is fixed and hardened, otherwise the delicate rugae of the mucosa are disturbed. Small, flat, roughly circular disks, about the thickness of a five cent piece result.

The Ovary.—The best incision is one extending from pole to pole, bisecting the organ parallel to its flattened surfaces. Small segments are then cut from selected areas, perpendicular to the main incision.

Small cysts may be sectioned entire. Only portions of the wall of larger cysts are selected. Large tumors are usually bisected or partly cut through in numerous places in order that differences in gross appearance can be noted. From the various locations pieces are removed for embedding.

Size of Pieces.—For frozen sections or rapid paraffin embedding pieces 1 cm. by 1 cm. by 0.3 cm. are best. Paraffin sections 3 by 2 cm. in size are not difficult to obtain from suitable and well-embedded material. There is no limit to the size of the blocks which can be cut with the celloidin method, the length of the microtome bed and the knife blade determining this.

Old safety razor blades will be found most useful in cutting out pieces of tissue, as these blades are very thin and sharp, and can be constantly

replaced when they grow dull. Thick-bladed knives, particularly if not sharp, bruise and distort along the line of incision.

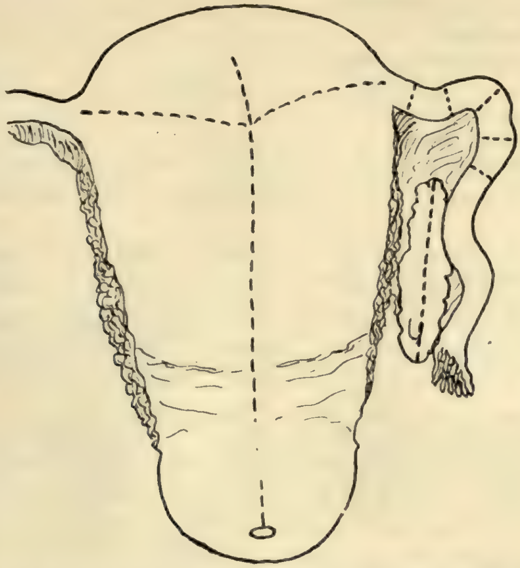

FIG. 3.—DOTTED LINES INDICATE PROPER SITES FOR LAYING OPEN THE UTERUS, AND CUTTING THE TUBE AND OVARY.

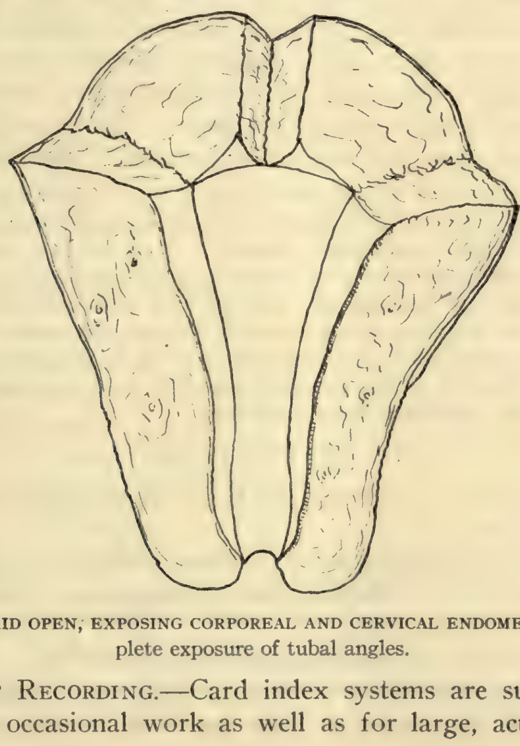

FIG. 4.—UTERUS LAID OPEN, EXPOSING CORPOREAL AND CERVICAL ENDOMETRIUM. Note complete exposure of tubal angles.

METHOD OF RECORDING.—Card index systems are sufficiently elastic to be used for occasional work as well as for large, active institutions.

The following outline plan can be modified to meet all requirements. Two sets of cards are used.

White—operative and diagnostic.
Blue—autopsy material.

White.—These entry cards contain:

Name............ Ward........... Date............ Physician............
Source of material..
Macroscopic Diagnosis...
Microscopic Diagnosis...
Pathological No.............(The numbering of the slides corresponds to this.)

Blue:

Name.................................. Date........................
Clinical Diagnosis..
Pathological Diagnosis..
Pathological No......................Page in autopsy book...............

Both sets of cards are, of course, cross indexed, one for the name, one for the disease.

In a separate cabinet a similar set of cards is kept of all microscopic slides, the one indexed under names, the other under diseases, regions, etc. A short description of each slide is recorded immediately after it is examined. Findings of special interest are cross indexed as—"*foreign body giant cells*," "*mitoses* in alveolar carcinoma," "*hyaline degeneration* of blood vessels in uterine fibroid," etc., according to special requirements.

A system such as this is not only time saving and business-like, but invaluable for reference, the proper utilization of material, and for scientific work. Even though a case is definitely finished the slides should not be discarded. Years afterward new developments or inquiries from other sources may again require reference to them. The pathologist's reputation may depend upon these incontrovertible records. The following is a case in point:

Curettings from a patient were submitted for examination. The report returned was "endometrium with slight hyperplastic changes." Two and one half years later this patient died, the symptoms pointing to carcinoma of the liver. As uterine hemorrhage preceded her decease, the attending physician inclined to the opinion that carcinoma of the corpus uteri had been overlooked, and had metastasized in the liver. The sections obtained from the curettings were reexamined, and for confirmation submitted to other pathologists who agreed with the diagnosis made 2½ years previously. Thus both the gynecologist and the pathologist were exonerated.

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CHAPTER III

ANATOMY AND NORMAL HISTOLOGY OF THE FEMALE GENERATIVE TRACT

Large volumes have been written which deal exclusively with the anatomy of individual organs of the female generative tract (1). In this connection only a summary of such facts as are of use to the pathologist will be considered and for the details of surgical anatomy the reader is referred to other sources. The topics to be considered include a description of the genitalia of the adult, and of the variations occurring in childhood and after the menopause. The discussion has been largely limited to the stage of rest. The purely functional changes which take place in response to physiological demands (menstruation, pregnancy, etc.) are considered in the succeeding chapter.

The genitals may be divided into the external genitalia including the structures of the vulva, and into the internal genitals, embracing the vagina, uterus, fallopian tubes, ovary, epoöphoron, paroöphoron and pelvic connective tissues.

VULVA

I. **Gross Anatomy.**—*The gross anatomy of the vulva* can be briefly sketched in connection with Fig. 5.

The vulva is composed of the:

1. Mons veneris.
2. Labia Majora.
3. Labia Minora.
4. Clitoris.
   - Glans
   - Crura
   - Bulbus Vestibuli.
   - Prepuce.
   - Frenulum.
5. Vestibule.
6. Urethra
   - Periurethral ducts.
   - Paraurethral ducts.
7. Hymen.
8. Bartholinian Glands.

1. *The Mons Veneris* is the fatty prominence situated in front of the symphysis pubis. At puberty it becomes covered with crisp, curly hair, arranged so as to form a sharp border with its concavity upward. (In the male type the hair border extends upward toward the umbilicus in the shape of a triangle with base downward). The subcutaneous fat may be 2 to 8 cm. thick.

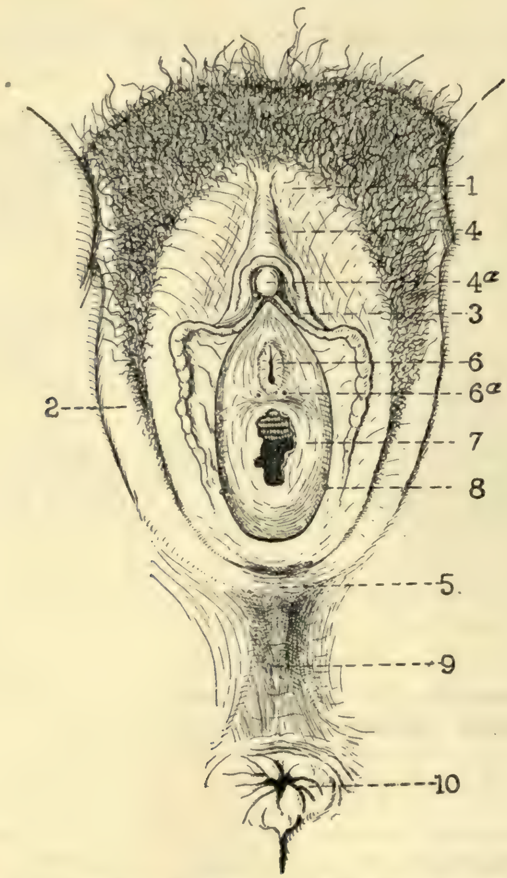


FIG. 5.—THE VULVA. SEMIDIAGRAMMATIC. 1. Mons veneris. 2. Right labium majus. 3. Left labium minus. 4. Clitoris. 4*a*. Glans clitoridis. 5. Fourchette. 6. Urethra. 6*a*. Paraurethral ducts. 7. Hymen. 8. Opening of bartholinian duct. 9. Skin surface of perineum. 10. Anus.

2. *The Labia Majora* are two folds of skin extending and merging above with the mons, below gradually becoming less prominent and uniting in the median line to form the posterior commissure (fourchette). Above and on their outer surface are numerous hairs. On the inner surface the skin is moist, soft and pinkish in color (7.5 cm. long, 2.5 cm. thick).

3. *The Labia Minora or Nymphae* are thinner and smaller folds, which above split into two layers to enclose the clitoris (prepuce, frenulum), and

below are lost, merging with each labium majus at about its middle. In the nullipara when the labia majora are in apposition, the small labia are hidden, except at their upper end. (2.5 to 3.5 cm. long, 1 to 1.8 cm. wide, 0.3 to 0.5 cm. thick). Great individual variations in size of the nymphæ are common.

4. *The Clitoris* is composed of a small cylindrical body (formed by union of the two deep-lying crura), capped by the acorn-shaped *glans*. The clitoris is situated at the lower border of the symphysis. The *body* is covered by the loose prepuce which leaves only the glans exposed. The *crura* diverge and lie deeply placed in apposition with the periosteum of the lower border of the pubic and ischiatic rami. (Glans 5 mm. in diameter, body 2 to 2.4 cm. long, crura 3.5 to 4 cm. long.)

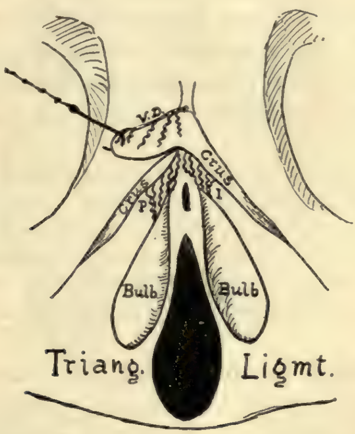


FIG. 6.—SEMIDIAGRAMMATIC REPRESENTATION OF CLITORIS AND ERECTILE TISSUE OF VULVA The clitoris, freed of its skin covering, is shown pulled toward the right side of the cadaver in order to expose the junction of the left crus and body of the clitoris. Urethra and vagina are in solid black. V.D. = vena dorsalis clitoridis. P.I. = pars intermedia (of Kobeld) which establishes the anastomosis between bulbs and crura.

Two further masses of erectile tissue, the *bulbi vestibuli*, lie to either side of the vaginal opening above the labia minora. Their vascular connections anastomose with those of the glans by means of the *pars intermedia* (length of bulb 2.5 cm.). (Fig. 6.)

5. *The Vestibule* is the space included between the labia minora and bounded above by the clitoris, below by the fourchette. Within this region are found the urethra, hymen and vaginal orifice, and the openings of the paraurethral and bartholinian ducts (Fig. 5).

6. *The Urethral Orifice* pierces the vestibule about 2 cm. below the clitoris. The opening which is usually situated upon a slight elevation (urethral papilla) is sagittal, crescentic, crucial or stellate. The average diameter is 5 mm. Immediately within the orifice, the lumen of the urethral canal expands. Hidden within the orifice are the openings of the bilateral

Periurethral Ducts (Skene's ducts) narrow canals which run inward for 0.5 to 3.0 cm. in the lateral posterior urethral wall.

The Paraurethral Ducts are two small and inconstant canals opening below and slightly external to the urethral papilla, and running inward for a short distance. (0.2 to 1.0 cm.)

7. *The Hymen,* which appears as a continuation of the posterior vaginal wall, is the membrane separating the vestibule from the vagina. The hymen is higher posteriorly toward the fourchette than anteriorly. Great variations in thickness, size and shape of its opening are the rule (annular, crescentic, cribriform, etc.). Coitus and childbirth injure the hymen. The shrunken nodules, remains of this structure, found around the vaginal orifice, are known as the *carunculae myrtiformes.*

8. *The Batholinian Ducts* open on each side in the groove between the hymen and labium minus, at about the posterior third of the lateral boundary of the vaginal wall. Each minute opening (0.5 to 0.6 mm.) leads into a duct 1.5 to 2 cm. long which passes backward and outward to the deeply situated gland (glandulae vestibulares) 1.5×2 cm. in size.

In infancy and before puberty the vulva is proportionately smaller than in the adult. The mons and labia majora contain little fat and the hair is scant and almost invisible (lanugo). The color of the structures included between the labia is very light pink.

After the menopause all the structures of the vulva atrophy. Both labia are reduced in size and become flabby and pale. The hair of the mons becomes gray and may fall out. The entire vulva presents a shrunken, parchment-like appearance.

II. **Normal Histology of the Vulva.**—1. *Labium Majus* (Fig. 7). The outer surface of the labium corresponds to that of the skin found on other hairy parts of the body. A superficial epithelial layer (epidermis) *composed of stratum corneum* (flattened horny cells, nucleus absent in outer layers) and *stratum germinativum* (prickle cells next to horny layer, then spherical cells, and lastly cylindrical cells with oblong nuclei). The superficial portions of the germinative layer contain pigment granules (stratum granulosum). Below the epidermis is the *true skin* (corium, derma) which harbors various epithelial derivatives (hair, sweat and sebaceous glands). The corium is composed of a *papillary layer,* abutting against the epidermis, and consisting of wavy connective and elastic tissue, nerves, blood vessels, etc. The deeper portions of the papillary layer gradually merge with the reticular layer (a coarse meshwork of similar composition) which rests upon the subcutaneous tissue.

Sebaceous glands are large and numerous. They are distributed in the superficial layer of the corium (Fig. 8). These are branched, simple, saccular glands composed of several lobules (5 to 7 in number, lined with low cubical or cylindrical epithelium, the lumen filled with degenerating cells) uniting to form a duct (stratified squamous epithelium) and forming appendages to the large

Hairs.—The hairs spring from hair follicles in the subcutaneous layer.

Sweat glands reach down to the subcutaneous layer, where they begin as a spherically coiled tube, which then runs straight upward toward the surface and pierces the epidermis. (Unbranched tubular glands; fundus with single cubical epithelium containing fat droplets; duct, stratified cubical epithelium; fine membrana propria.)

The subcutaneous layer of the labium contains much fat and some unstriped muscle (tunica dartos). At the upper pole of the labium the round ligament of the uterus spreads out and blends with labial tissues.

The inner surface of the labium is soft, moist, without hair. The sweat glands on the inner surface run nearly parallel to the skin surface.

The labium in infancy contains less fat. The epidermis is thinner, the hair is fine, scantier and appears as a mere appendage to the sebaceous

FIG. 7.—LEFT HALF OF VULVA: NEWBORN (×7). 1. Labium majus showing surface epithelium, hair follicles, a few hairs projecting slightly beyond the surface and connective tissue. 2. Labium minus. 3. Hymen showing external and internal surface. 4. Muscle fibers and connective tissue septa running into labium majus. 5. Fat.

glands. The senile labia are atrophic. Their epidermis is very thin. The ducts of the sebaceous glands are dilated; the alveoli are smaller and nearly tubular, having lost their plump configuration.

2. *The Labium Minus* is a skin fold covered by a layer of stratified squamous epithelium, like that of the large labium but thicker. There is a central core of loose connective and elastic tissue, rich in blood vessels (venous plexuses), containing some involuntary muscle fibers. There are no hairs, few sweat glands, but many sebaceous glands which spread fan-like beneath the surface. Nerve endings are numerous, some fibers ending free in the epithelium, others terminating in end organs.

These end organs are mainly of three kinds (Moraller and Hoehl, Webster):

Vater Pacinian Corpuscles composed of concentric lamellae (0.5 to 1.5 mm. in length) enclosing a nerve fiber. They lie deep in the stratum reticulare.

End Bulbs of Krause appear as irregularly spherical bodies containing a naked axis cylinder, which breaks into branches and varicose fibrils (0.002 to 0.05 mm. in diameter).

Meissner's Corpuscles, found in the summit of the papillae of the corium; irregular ellipsoid bodies within which the axis cylinder winds in wavy spirals (0.12 to 0.18 mm. long).

In infancy the sebaceous glands are absent or few in number. They may increase by the sixth to seventh year, but are usually not numerous before the tenth to twelfth year. *In the aged* the entire labium atrophies. The sebaceous glands disappear almost completely and are usually represented by blunt epithelial tubular depressions or small collections of round cells underneath the surface of the epithelium.

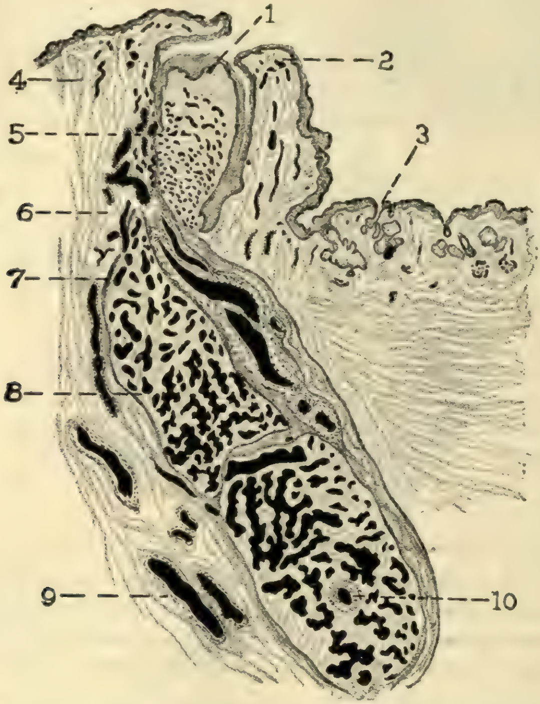


FIG. 8.—OBLIQUE SECTION PASSING THROUGH CLITORIS, LABIA, RIGHT CORPUS CAVERNOSUM: NEWBORN (×12). 1. Glans clitoridis covered by squamous epithelium. On each side the preputial folds embrace the glans. On the right the deep sulcus coronarius appears in the plane of the section. 2. Prepuce merging into labium minus. 3. Right labium majus showing sebaceous and sweat glands. The dotted line points to the opening of a sebaceous gland. 4. Part of left labium majus. 5. Corpus clitoridis. Veins shown in solid black. 6. Anastomosing veins communicating with corpus, crus and bulbus clitoridis (plexus intermedius—see Fig. 6, P. I.). 7. Tunica albuginea of right crus clitoridis. 8. Cavernous tissue of crus. 9. Large veins. 10. Artery supplying crus.

3. *The Clitoris* (Fig. 8). The corpus, crura and bulb are composed of cavernous tissue enclosed in a firm connective tissue sheath. The glans has a similar composition but as it projects free it has an additional covering consisting of a thin layer of skin. The prepuce has the same composition as the nymphae, by which it is formed, containing at its point of reflexion (sulcus) sweat and sebaceous glands and nerve endings (inner surface).

4. *The Urethra* (Fig. 9) consists of an inner epithelial layer and an outer muscular tunic. *Skene's ducts* (the periurethral ducts) end just within the orifice. The urethra contains a few simple mucous glands.

The urethral *epithelium* is commonly a stratified squamous epithelium. It may, however, be stratified transitional (Fig. 9) or even stratified cylindrical in type. The epithelium rests upon a fine cellular connective tissue, which at the orifice forms papillae.

The unstriped muscular coat consists of an inner circular and outer longitudinal bundles. Between the bundles are many veins (corpus cavernosum urethrae) and much elastic

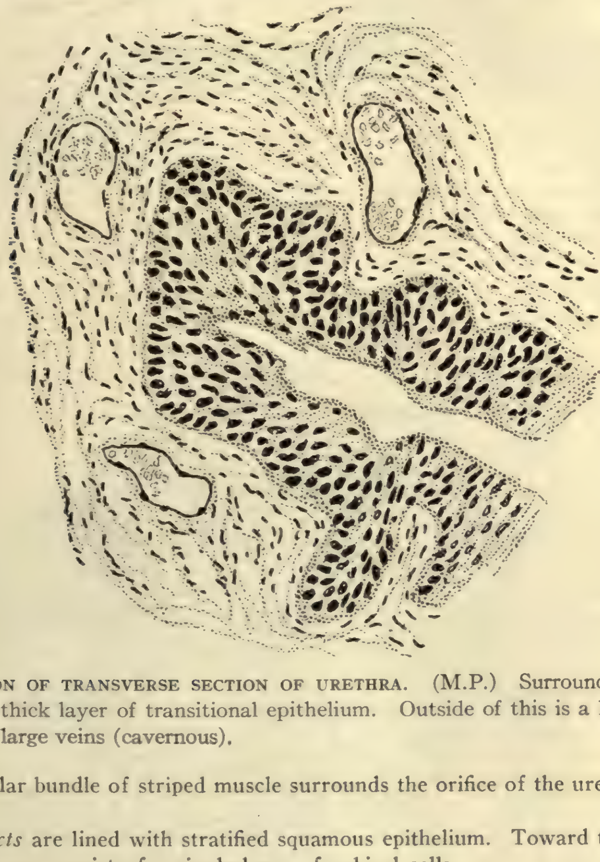


FIG. 9.—PORTION OF TRANSVERSE SECTION OF URETHRA. (M.P.) Surrounding the central lumen is a thick layer of transitional epithelium. Outside of this is a loose connective tissue with large veins (cavernous).

tissue. A circular bundle of striped muscle surrounds the orifice of the urethra (sphincter externus).

Skene's ducts are lined with stratified squamous epithelium. Toward their blind ends the epithelium may consist of a single layer of cubical cells.

5. *The Hymen* (Fig. 10) is a connective tissue membrane lined on both sides by stratified squamous epithelium. In the connective tissue run many blood and lymph vessels, and nerve endings are numerous. The carunculæ myrtiformes have the same structure as the hymen.

6. *The Bartholinian Glands* are compound alveolar glands (Fig. 11). The terminal alveoli are lined with high cylindrical epithelium and goblet cells. The alveoli are grouped in grape-like clusters (lobules) enclosed by connective tissue septa traversed by unstriped muscle fibers. The smaller

ducts are lined by simple cubical epithelium (Fig. 12). Between the larger collection of lobules are broader septa composed of fibrous and muscular

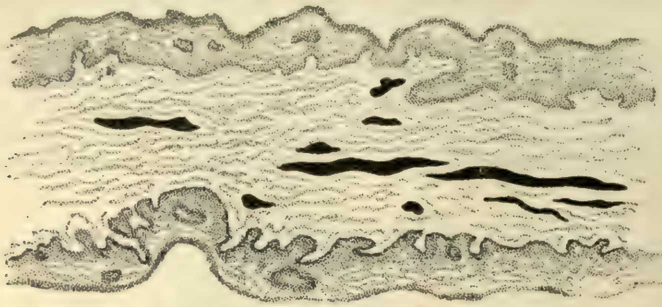


Fig. 10.—Cross section of hymen of adult woman. (L.P.) The upper layer of stratified squamous epithelium faces toward the vagina, the lower layer externally. Between the two is a firm stratum containing connective tissue, elastic fibers, nerves and vessels. Large vessels in solid black.

(striped and unstriped) tissue. The main duct is lined by stratified cylindrical epithelium, but at its termination by stratified transitional or squamous epithelium. Numerous small mucous follicles empty into this duct.

Fig. 11.—Section of Bartholinian gland. (M.P.) Numerous alveoli, lined by a high cylindrical epithelium, which rests on a well-defined basement membrane, are grouped about a central duct. Secretion in lumen of alveoli and duct.

In infancy these glands have the same composition as in the adult, but are only one-half the size. The other structures also differ but little, except in size, from those of the adult.

In old age.—The bartholinian glands undergo atrophy.

THE VAGINA

I. **Gross Anatomy.**—The vagina is a slightly curved tube which leads from the uterus to the exterior of the body. It functionates as

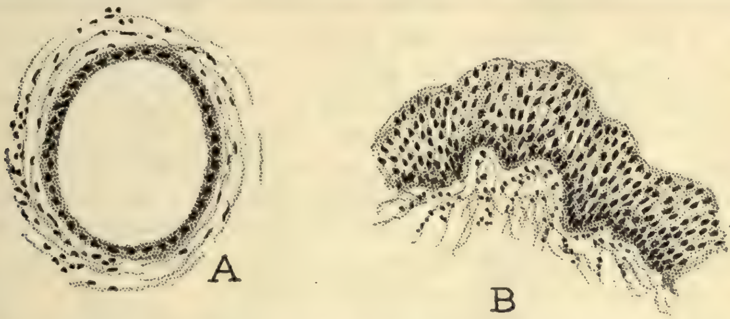


FIG. 12.—BARTHOLINIAN GLAND. (H.P.) A. Small duct of bartholinian gland, lined by low cuboidal epithelium. B. Portion of transitional epithelium lining main duct of bartholinian gland.

the lowest portion of the excretory system of the ovary, and also serves as the organ of copulation.

The fact that the vagina is curved with convexity directed backward, and that the portio vaginalis (infravaginal part of the cervix) is set

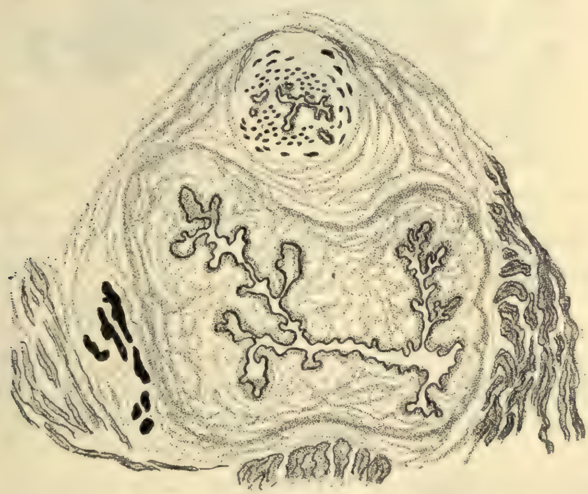


FIG. 13.—HORIZONTAL SECTION PASSING THROUGH LOWER VAGINA AND URETHRA: NEWBORN. (×7.) Above, urethral lumen surrounded by cavernous sheath. Middle, H shaped vaginal lumen. Below, longitudinal muscle fibers of rectal wall. Laterally, puborecta fibers of levator ani cut obliquely.

obliquely in the vaginal vault (pointing downward and backward) accounts for the greater length of the posterior vaginal wall (8.5 to 10 cm.) compared to that of the anterior (7 to 8 cm.). (See Fig. 14.)

The outer opening (orificium vaginae) is the narrowest part. It is still further contracted by the hymen. The walls of the vagina are in apposition. The intermediate portion is wider and has a |><| or |——| shaped cross-section. Transversely the vagina measures 2.5 cm. in this portion (Fig. 13). The upper portion expands to enclose the cervix, forming the vault, a nearly annular groove. Posteriorly this groove is deeper (posterior fornix), anteriorly it is shallow (anterior fornix). The upper 1.5 to 2 cm. of the posterior fornix comes into contact with a triangular area of peritoneum, the lowest part of Douglas' cul-de-sac. The remainder of the vagina is surrounded by loose areolar tissue (paravaginal tissue).

The vaginal surfaces are elevated into folds. An anterior ridge, which may be double, and a posterior median ridge, both run sagittally (Fig. 15). From these median columns dentate transverse folds, growing less marked as they approach to the lateral walls, diverge.

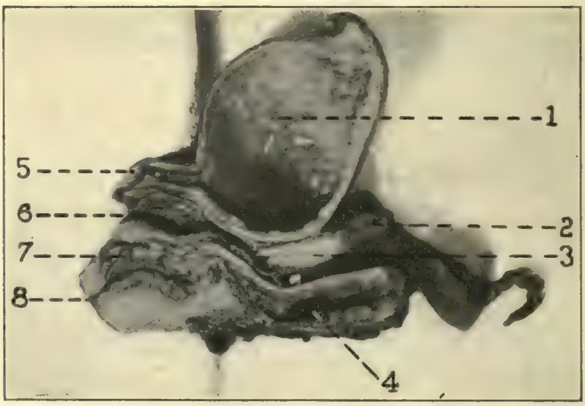


Fig. 14.—Sagittal median section of pelvic viscera of a child. Hardened in situ (reduced). 1. Interior of bladder. 2. Small corpus uteri. 3. Large infantile cervix. 4. Lumen of rectum. 5. External opening of urethra. 6. External opening of vulva. 7. Perineal body. 8. Anus.

* Lowest part of Douglas' cul-de-sac.

The color of the mucosa is a whitish red. The surface is moist, and, normally has whitish to yellowish crumbly masses (desquamating epithelium, cervical mucus, etc.) adherent to it. The wall of the vagina is 2 to 3 mm. thick.

II. **Normal Histology of the Vagina.**—Three distinct layers may be recognized—epithelium, subepithelial connective tissue, muscle. Some authors describe the paravaginal tissue as an additional layer (adventitia).

The Epithelium is stratified, squamous in type (0.15 to 0.2 mm. thick), and resembles that of the skin, except that the horny layer is absent. The cylindrical cells (matrix) adjacent to the subepithelial tissue is considered as a *membrana propria* by some. Superficial to this is a thicker layer of

large polygonal cells, and the surface is covered by longitudinally disposed, desquamating cells.

The Subepithelial Connective Tissue (tunica propria) consists of a fine meshwork of connective tissue and elastic fibers. In it run many vessels, especially plexiform veins, lymphatics and nerves. This tunic shows numer-

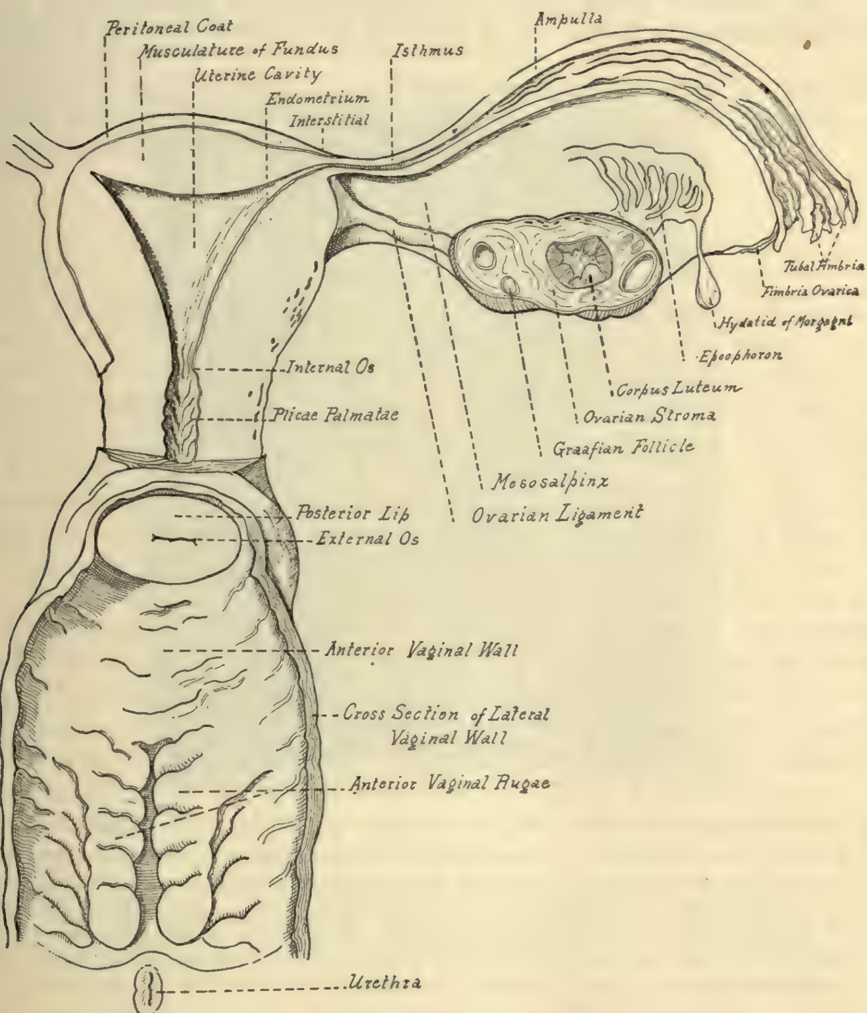


FIG. 15.—CORONAL SECTION OF FEMALE GENITAL TRACT SHOWING RELATIONS OF ALL THE STRUCTURES. Semidiagrammatic (modified from Henle).

ous papillary elevations which serve to raise the vaginal surface into folds, though part of the projection is offset by the fact that the epithelial covering is thinnest at the apex of these rugae. The subepithelial connective tissue which forms the main rugae is almost cavernous in type, because of its great wealth in large veins.

The Muscle.—Some authors describe but a single longitudinal layer; others recognize two not plainly defined layers—an inner circular and outer longitudinal. The muscle fibers are unstriped.

Nerve fibers run in the musculature, giving off branches at right angles, which subdivide and penetrate to the epithelium.

The lymphatics of the upper two-thirds form a fine network in the subepithelial connective tissue. They assemble to unite into two trunks which

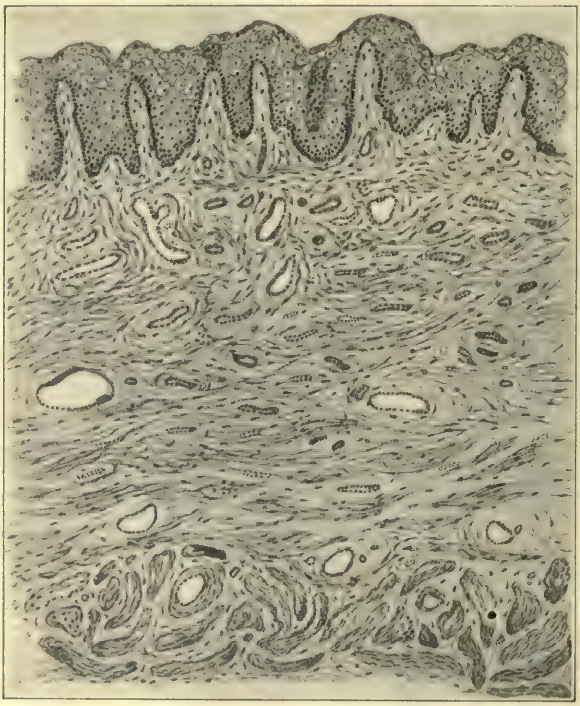


FIG. 16.—TRANSVERSE SECTION OF VAGINA OF YOUNG WOMAN. (M.P.) Above (lining the lumen) is the epithelial layer composed of thin, desquamating surface cells, next polygonal cells, and adjacent to the subepithelial tissue a row of cylindrical cells. Intermediate is the tunica propria showing papillae at the epithelial border. The tunic is composed of strong connective tissue, many elastic fibers and harbors blood vessels and nerves. Below (toward the paravaginal tissue) is unstriped muscle in ill-defined circular and longitudinal distribution.

course upward on the posterior wall, join the superior hemorrhoidal vessels, surround the rectum and empty into the superior hemorrhoidal and mesorectal glands, Bruhus (3). The lower third drains into the inguinal glands.

Lymph follicles occur particularly in the upper half of the vagina. They lie beneath the epithelial layer.

Glands are but rarely found. v. Preusschen (4) has described them in adults (like sebaceous glands); Robert Meyer (5) in infants. The latter

are cervical in type (ciliated cylindrical epithelium lining simple or compound tubular glands).

In Infancy the epithelial layer is thicker than in the adult, the transverse rugae are accentuated and the subepithelial connective tissue is finer in structure and contains very little elastic tissue (Fig. 13).

In old age, the atrophy shows itself in the diminished thickness of the epithelial layer and muscle, effacement of the rugae, and increase in the density and amount of subepithelial connective tissue.

The fornix is more or less obliterated, keeping pace with the shrinkage of the cervix, and is distorted by bands, or by agglutination of opposing surfaces (so-called "senile vaginitis"). (See p. 141.)

THE UTERUS

I. **Gross Anatomy.**—Position.—The adult uterus is a pear-shaped hollow muscular organ which below is inserted at nearly a right angle into the upper anterior wall of the vagina, and above is continuous on either side with the fallopian tubes. The lower segment of the uterus is firmly fixed in the pelvis by means of the parametria. In the adult the portio vaginalis lies slightly posterior to the mid-axis of the pelvic cavity at a level corresponding to a line drawn between the two ischial spines. The upper segment of the uterus is mobile. In the anteflexed position it forms an obtuse angle of 135° (open in front) with the cervix (Winter l. c. 1).

Size.—The size of the uterus differs not only in the nulliparous and parous women, but also varies according to the time relation to menstruation. In the resting stage (4 to 10 days after menstruation) the *nulliparous* organ is 7 cm. long, 4 cm. wide (at the site of the insertion of the tubes), and 2.5 cm. thick. Two and one-half cm. of the length are represented by the cervix. The parous uterus measures 1 cm. more in every diameter, except the longitudinal (7 cm. long, 5 cm. wide, 3.5 cm. thick).

Weight.—The nulliparous uterus weighs on the average 40 to 50 g.; the parous 60 to 70 grams.

The Walls.—The corpus uteri is flattened from before backward, the anterior surface being less rounded than the posterior. The fundus which corresponds to the portion above a line connecting the two tubes is arched. The fundus and posterior wall are the thickest parts of the uterus (1 to 1.5 cm. in nulliparae, 2 cm. in parous women). At the tubal angles and in the cervical canal the walls are not more than 8 or 9 mm. thick.

The Cavity of the Uterus (Fig. 4, p. 15) is flattened sagittally, so that its anterior and posterior walls are nearly in contact. The outline of the cavity forms a triangle with base directed upward, and the apex continuous with the fusiform cervical canal. The lateral walls and base do not run in straight lines, but are curved inward by the projecting uterine walls. The length of the cavity from the external os to the fundus is from 6 to 7 cm.;

its greatest width is 2.5 cm. The capacity of the undistended uterus is from 3 to 5 c.c.

Peritoneal Investment.—The peritoneum is firmly attached to the anterior wall of the uterus down to the level of the internal os in the median line. Laterally the line of firm attachment passes in an upward curve to just below the junction of the round ligaments with the uterine horns. Posteriorly the peritoneum invests not only the entire uterus, but extends downward for 2.5 cm. upon the posterior wall of the vagina. Laterally, from the tubes downward, an area, narrow above and gradually broadening below, is devoid of peritoneum. This uninvested strip corresponds to the attachments of the broad ligaments and of the upper part of the lateral parametrium. Through these spaces the vessels, nerves and lymphatics reach the uterus.

Divisions.—Not only for the sake of convenience, but also because they correspond to well-defined anatomical, histological and clinical differences, the uterus has been divided into the following segments:

1. Corpus uteri.
2. Isthmus (Aschoff).
3. Cervix { Supravaginal
Infravaginal (portio vaginalis).

Fig. 17.—Transverse section through fundus of uterus of newborn. (×7.) The intestinal part of the tube has been cut twice on each side by the plane of the section. Note slit-like lumen of uterine cavity.

1. *The Corpus Uteri* represents the upper half of the entire organ. It is the thick-walled muscular portion destined to harbor, nourish and expel the ovum (Fig. 15). The consistence is firm and resilient. A thin, glistening, peritoneal coat forms its covering. Internal to this is the thick pinkish muscular layer in which large vessel-lumina are prominent. The lining of the cavity (endometrium) is moist, smooth and of deeper pink color. It is firmly attached to the muscle. At the tubal angle the endometrium grows thinner and is continuous with the mucous membrane of the tube (Figs. 15 and 17).

2. *The Isthmus* is not recognized as a separate entity by some anatomists. It is the intermediate zone between corpus and cervix, usually situated below the internal os and extending downward for 6 to 8 mm. (Aschoff, Hegar (7)). Though of much importance theoretically (placenta

previa, cervical implantation lower uterine segment in labor), it often cannot be demonstrated grossly, and not always microscopically (Fig. 19).

3. *The Cervix* is the mainly fibrous (passive) part of the uterus. The supravaginal portion as its name implies, is situated above the attachment of the vagina. The infravaginal portion is the rounded eminence which

FIG. 18.—SAME AS FIG. 17 THROUGH MIDDLE OF UTERINE BODY. Lumen shorter and more circular. Note entrance of uterine vessels on left side.

projects into the vagina. The cervical canal extends from the external to the internal os (unless the isthmus encroaches downward), and establishes communication between the vagina and uterine cavity.

The infravaginal portion of the cervix (portio vaginalis or portio for short) points forward and downward. It consists of two lips, an anterior

FIG. 19.—SAME AS FIG. 17 AT LEVEL OF ISTHMUS.

lip which is shorter, broader and lower than the corresponding posterior one. The external os lies in a small dimple, and is approximately 5 mm. in its longest (transverse) diameter. In women who have had children the external os shows more plainly, because of lacerations, which accentuate the division into anterior and posterior lips. The portio has a red violaceous color, its surface is smooth. The consistence of the portio is firm, like that of soft cartilage.

The supravaginal portion has a firm, fibrous wall. There is no peritoneal investment, except posteriorly. The mucous membrane lining the cervical canal during life has a bright red color, and is thrown into folds. These folds form an anterior and posterior column with upwardly diverging branches arranged like the sticks of a fan, radiating from above the external os and extending to the internal os (arbor vitae or plicae palmatae). The internal os is the most contracted part of the canal (diameter about 1 mm.).

At birth the uterus is only 3 cm. long. The cervix occupies ⅔ of this length; so that the small corpus appears as a mere appendage to the cervical segment. The cervical

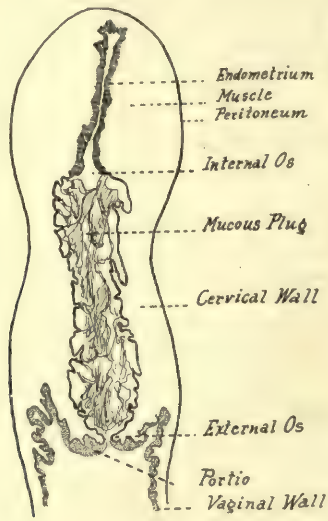


FIG. 20.—LONGITUDINAL, SAGITTAL SECTION OF UTERUS OF NEWBORN. (×2.) The proportion of cervix to body (1,5 : 1) normal at time of birth is shown. Cervix dilated by mucus.

canal is often greatly dilated by retained mucus (Fig. 20). The portio is small, and the internal os poorly defined. The arched fundus is lacking in the infant uterus. At birth the upper limit of the uterus lies at the level of the fifth lumbar vertebra (Merkel). By the sixth year the external os lies at the level of the ischial spines as in the adult (Symington).

After the menopause there is a gradual atrophy of the uterus. The cervix is particularly affected. In old age it may shrink, and appear as a mere dimple high up in the contracted conical vagina. The entire uterus becomes pale and flabby, the muscle layers and mucosa both showing diminution in thickness. The uterine cavity is first slightly enlarged (atrophy of muscle) and then greatly reduced in capacity (5 cm. in length).

II. **Normal Histology of the Uterus.**—THE ADULT UTERUS.—Just as in the gross description, the division into corpus, isthmus and cervix will be adhered to.

A. *The Corpus Uteri* consists of three layers—the endometrium, myometrium and perimetrium. *The Endometrium* (mucosa corporis) is from

0.5 to 1.0 mm. thick. It is composed of surface epithelium, stroma, glands, etc. *The surface epithelium* consists of a single layer of columnar epithelial cells with ciliary margin. In spots the cilia may be absent. Their movement is downward, toward the vagina. The large oval nucleus of the cells is nearly median in position. The protoplasm accepts a faint basic (nuclear) stain at all times except just before menstruation; only in the premenstrual time do acid (protoplasmic) dyes affect it. The epithelial cells are slightly shorter (20 to 30μ in height) than those of the uterine glands (Fig. 21).

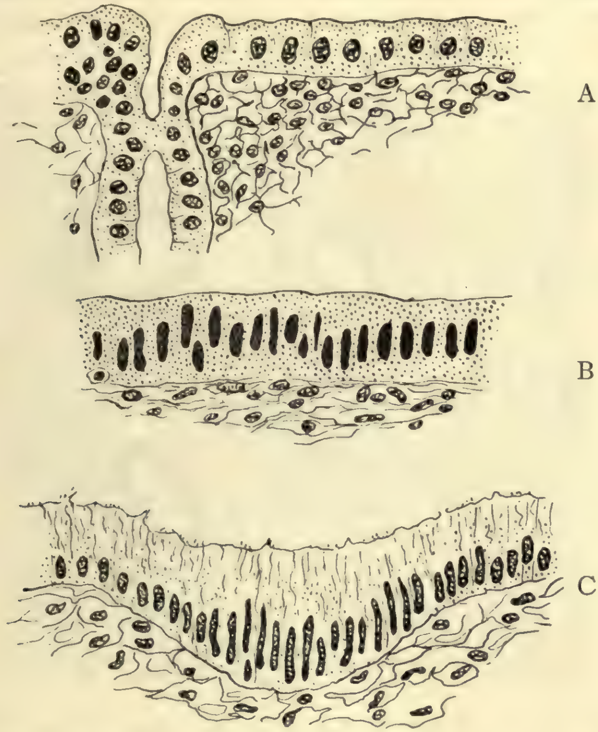


FIG. 21.—EPITHELIUM OF CORPUS, ISTHMUS AND CERVIX UTERI. (H.P.) A. Epithelium of corpus. Cuboidal cells with central oval nucleus; cytoplasm acidophile or basophile according to functional state. Cilia not shown. B. Epithelium of Isthmus. Cells low columnar to cuboidal. Nucleus central, cytoplasm variable as to staining qualities. C. Epithelium of cervix. Cells high columnar, nucleus basal, cytoplasm clear.

A *basement membrane,* showing occasional oval nuclei, arranged parallel to the uterine surface, separates the surface epithelium from *the stroma.* This layer, usually designated as cytogenic or lymphadenoid, is composed of three varieties of cells, a *branching network* (Fasernzellen) of interlacing cells resembling embryonal connective tissue. Within their meshes lie round and spindle cells. The *round cells* have a prominent deeply staining nucleus, and exceed in number the *spindle cells,* which are arranged chiefly about the glands and blood vessels. The protoplasm of both varieties of cells is min-

imal in amount, and can but rarely be demonstrated. The nuclei are about the size of red blood cells (7μ).

The demarcation between stroma and musculature is well defined, though the junction represents a wavy irregular line due to penetration between the subjacent muscle bundles. Collections of lymphoid tissue are seen in normal endometria (Fig. 22). Schroeder (6) found 7 in 120 cases. *The glands* are simple or bifurcated tubules 1 to 2 mm. long, about 40 to 50μ in diameter, and 0.1 to 0.2 mm. apart (i.e., separated by a distance of 4 or 5 gland diameters). They run nearly perpendicular to the surface, except at their fundus, where they frequently bend sharply and run parallel to the

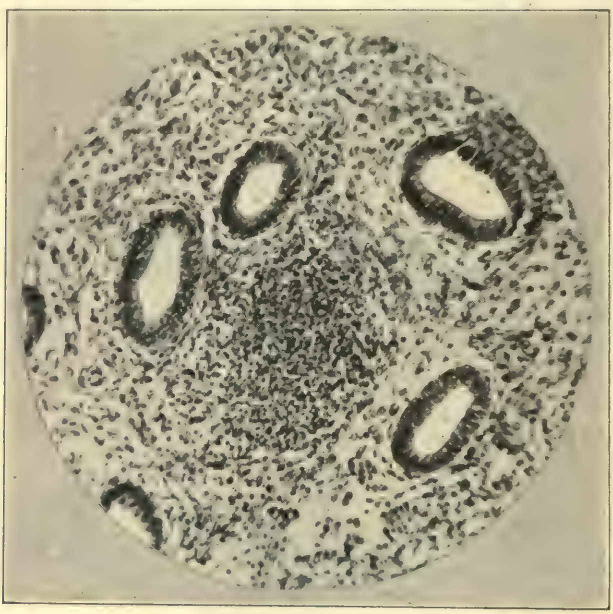


FIG. 22.—LYMPH FOLLICLE IN ENDOMETRIUM. (Photomicrograph, H.P.) Transverse section of uterine glands in resting stage. In center is lymph follicle.

muscle layer for a short distance. The fundi of some glands lie between smaller muscle bundles. There is a slight constriction of the lumen close to the mouth of the glands (neck). *The gland epithelium* is simple columnar ciliated in type, often higher than that of the surface (30μ). The cells secrete alkaline mucus. The gland epithelium rests upon a well-defined basement membrane.

The Muscle (Myometrium).—Attempts to separate the musculature of the human uterus into well-defined layers have failed. The intimate interlacing of innumerable bundles nullifies any such schematization. Nevertheless, three zones which differ in their main characteristics can be recognized. From within outward they are as follows:

1. *Stratum submucosum,* mainly small longitudinal bundles, between which appear small vessels. This layer is narrow.

2. *Stratum vasculare* consisting of circular and transverse bundles between which are contained many large vessels. This layer is thicker than the other two layers combined.

3. *Stratum supravasculare,* divisible into two parts, in which the bundles of the internal portion run both longitudinally and circularly, and of the outer part (stratum subserosum, Moraller and Hoehl) mainly longitudinally, and firmly bound to the peritoneum.

A connective tissue framework knits individual bundles together, and finer strands penetrate into the interior of the fasciculi. Cross sections, at various angles, produce the so-called *muscle rhomboids.*

The individual muscle cells are unstriped and of various shapes—elongated, spindle shaped or short and broad. Their length is from 40 to 60μ. Cut transversely the cells appear round, ovoid or polygonal, somewhat like a red blood cell, but with less defined outline. The nucleus is ordinarily rod-like, but if fixed during contraction of the fiber it is sickle or half-moon shaped. On transverse section many cells appear to contain no nucleus (nucleus above or below the plane of section).

The Serosa (peritoneal coat, perimetrium) consists of a single layer of flat endothelial cells with spindle-shaped nuclei. Where it is firmly attached, muscle fibers spring from the peritoneal membrane itself. Where the peritoneum is more movable a fine, avascular connective tissue is interposed.

B. *The Isthmus Uteri,* according to Hegar (7) sometimes encroaches upon the lower part of the uterine body, more often it is below the internal os (os anatomicum). This segment shows both cervical and corporeal properties. It has the same layers as the body of the uterus. The muscle is less abundant than in the corpus, but more plentiful than in the cervix. The surface epithelium is endometrial in character, the glands also are like those of the corpus, though shorter than at the fundus of the uterus. Short cervical and corporeal glands often occur intermingled (Fig. 21B). The thickness of the entire mucosa is considerably reduced. The lower boundary of the isthmus can be defined only by histological examination (os histologicum). Whether this new subdivision will be generally accepted by anatomists remains to be seen.

C. *Cervix Uteri.*—(a) *Supravaginal portion and cervical canal.*

The cervical mucous membrane, because it is thrown into folds, presents a large surface. It is firmer and more fibrous than that of the corpus. From the isthmus to the external os the mucosa is identical in character, irrespective of the gross division into supra and infravaginal portion. Beyond the external os the mucosa resembles that of the vagina.

The surface epithelium above the external os is composed of a single layer of high, slender columnar ciliated cells (40μ by 4μ). Their oval nucleus is basal. The protoplasm does not stain with basic dyes (stains with muci-carmine), hence the contrast between the pale cell body and deeply colored nucleus is striking. A well-defined basement membrane can be demonstrated.

The glands are simple or compound tubular with wide mouths (0.3 to 0.4 mm. in diameter (Henle)). Not infrequently they are branching, and when dilated present pictures approaching the alveolar type. Other glands

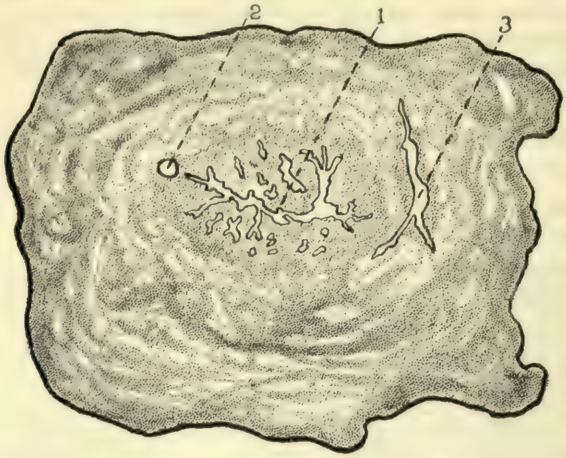


FIG. 23.—TRANSVERSE SECTION OF SUPRAVAGINAL PORTION OF CERVIX. (L.P.) 1. Central lumen of cervix with branching cervical glands. 2. Gaertner's duct. 3. Dilated Gaertner's duct of opposite side.

are mere depressions of the surface epithelium. The gland cells are high, columnar ciliated epithelium, similar to those of the surface. Their lateral boundaries are often indistinguishable. The cells rest upon a basement

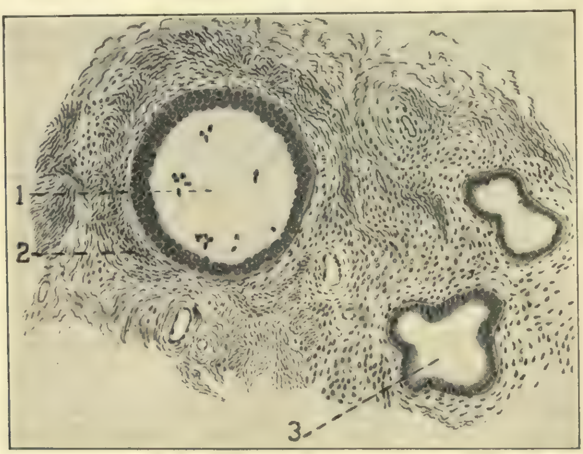


FIG. 24.—ENLARGED PORTION (2) OF FIG. 23. (M.P.) 1. Gaertner's duct lined by low cuboidal epithelium, leucocytes in lumen. 2. Irregular bundles of unstriped muscle surrounding duct. 3. Cervical glands.

membrane. The gland lumina and usually the cervical canal contain a thick glairy mucus mixed with desquamating cells and detritus. Small macroscopic cystic bodies, varying in size from that of the head of a pin to that

of a pea occur within the canal and in the portio. They represent closed dilated glands (Ovula nabothi). (See Fig. 141, p. 198.) The epithelial lining of these cysts is low columnar, even cuboidal; their contents is cervical mucus.

The cervical connective tissue appears to radiate in fan shape from a central point at the level of the insertion of the vagina into the cervix (Moraller and Hoehl l. c. 1). There are many elastic fibers. The tissue compared with that of the stroma of the uterine mucosa is very poor in cells and nuclei.

The cervical musculature is scant, and distributed in two longitudinal layers, an internal and an external one, the latter continuous with the uterine and vaginal musculature. Besides this there is a middle circular layer most strongly developed in the vicinity of the internal os. The fibers are smaller than those of the uterus.

(b) *The Infravaginal Portion* (*Portio*). — The mucous membrane resembles that of the vagina. Its surface is, however, quite smooth. There are no glands.

The epithelium, which can be divided into three layers—an inner cylindrical (germinative), a middle broader stratum consisting of polygonal cells, and an outer flat desquamating—rests upon loose subepithelial connective tissue. Normally this stratified squamous epithelium ends abruptly at the internal os and is sharply demarcated from the brighter red cervical mucous membrane. Under certain conditions (see Chapter VII, p. 198) the cervical mucosa grows downward over part of the surface of the portio (erosion). In parous women, if the cervical canal becomes patulous, or exposed on account of laceration (eversion, ectropion) the squamous epithelium invades the cervical canal, replacing the cylindrical cells for a variable distance.

The connective tissue is fibrous, forms loose bundles and contains few nuclei. The connective tissue immediately beneath the epithelium is elevated into papillae. In the connective tissue are harbored many vessels, especially veins and venous radicles which ramify below the epithelium.

Muscle fibers appear only along the course of the larger vessels.

THE INFANTILE UTERUS.—*a. Corpus.*—The endometrium is thin. Its demarcation toward the muscle is poorly defined, but, as in the adult, consists of a wavy irregular line. The glands are represented by a few tubular depressions. The epithelium is cylindrical with an oval, often basal nucleus. A few goblet cells are found. *There are no cilia.* The basement membrane is developed. The stroma is cytogenic, consisting of the same varieties of cells as in the adult, but spindle cells are more numerous, and often are arranged in strands perpendicular to the surface. The musculature is also thin and is not divisible into layers. The small muscle fibers are intermingled with many fine spindle cells (undifferentiated muscle). The elastic tissue is poorly developed. It occurs about the large vessels in the inter-

muscular connective tissue, in the membrana propria, and subperitoneally (Moraller and Hoehl l. c. 1).

b. Isthmus.—Hegar (7) describes an isthmus in the infantile uterus. It is identical with that of the adult except that the epithelial cells are devoid of cilia.

c. The Cervix.—The cervical mucosa is lined by a higher cylindrical epithelium (20 to 60 μ) than in the adult. The nuclei are not so regularly basal; goblet cells are more common. The prominent plicae cause the epithelium to assume palisade or fan-shaped arrangements. Cilia are wanting. The glands are fewer in number and less regular in shape. Saccular, flask-shaped and antler-like forms occur. Ovula nabothi are often found. The connective tissue, arranged in three layers—an internal longitudinal, a middle circular, and an external longitudinal, overshadows the scant musculature even more than in the adult.

d. The Portio may show folds similar to those of the vagina. The squamous epithelium is thicker (more layers) than in later life. The papillae of the subepithelial tissue are few and small. The junction of squamous and cylindrical epithelium is most often at the external os. Quite frequently, however, the portio epithelium extends upward beyond this site. The cervical epithelium on the other hand, may extend upon the portio (congenital erosion) or, may lie exposed if the external os is everted (congenital ectropion).

THE SENILE UTERUS.—*a. The Corpus.*—*The mucosa* is thin and fibrous, The surface epithelium is low cylindrical or cuboidal and devoid of cilia

FIG. 25.—ATROPHIC ENDOMETRIUM AFTER ONSET OF MENOPAUSE. (H.P.) The surface epithelium is hypertrophic, and stratified in spots. The few glands present run parallel to the surface, the stroma is fibrous. 1. Surface epithelium. 2. Stroma and glands. 3. Muscle.

and the cell body takes an acidophile stain. The stroma shows a *predominance of spindle cells.* The glands, few in number, run obliquely or parallel to the surface (Fig. 25). They may be dilated or cystic. The

lining epithelium is low cubical without ciliary margin. Areas of epidermoidalization are not uncommon.

The muscle is atrophic, and appears strangled by large branching masses of connective tissue. The elastic tissue is not decreased. In extreme age it forms shapeless clumps, and loses its individual outline (Moraller and Hoehl).

The large arteries show typical senile sclerosis. Their internal elastic membrane splits up; new elastic tissue appears in the intima; the media necroses and calcifies, and many lumina are obliterated (Pankow (8)).

b. Ogata (9) describes an *isthmus* in the senile uterus. He claims that it shows characteristic senile changes and is often more plainly demarcated than in the adult.

c. The Cervix.—Although the cervix diminishes greatly in size, the changes in its epithelial constituents develop late. In very old women the cells may be flat, like endothelium. The cilia persist long after the menopause. The glands are few, often cystic, and lined with cuboidal or flat epithelium. In the stroma spindle cells predominate. The muscle atrophies. The large vessels show changes similar to those in the uterus.

Nerves, according to Roith (Monatsschft. f. Geburtsh. u. Gynäk., 1907, 25:79) for uterus and cervix arise from two sources—sympathetic (1 to 5th lumbar), and sacral autonomic (nervus pelvicus, 1 to 3d sacral). The ganglia of the sympathetic are in the inferior mesenteric, in the hypogastric plexus or in the cervical and uterine musculature. The ganglia of the n. pelvicus lie in the retrocervical connective tissue.

THE FALLOPIAN TUBES

I. **Gross Anatomy.**—The fallopian tubes are bilateral hollow muscular strands which connect the uterus with the ovaries. They differ from all other excretory ducts in that they are not in direct continuity with their secretory gland, the ovary, but merely in juxtaposition. Above the uterus, the internal genital organs retain throughout life their unfused bilateral form. They also represent the only communication in the body between a serous cavity, the peritoneum, and the outer world.

Position.—The fallopian tubes are not directly attached to any stable structures; they, therefore, cannot be said to occupy any fixed position. Mesially the tubes arise from the lateral angles of the uterus between, and slightly above the insertion of the round and utero-ovarian ligaments. With the uterus in an anterior position, the tubes run almost horizontally outward, until they reach the lateral pelvic walls. They then ascend slightly in front of the corresponding ovary, arching backward above this gland, and finally turn downward and inward behind the ovary, the fimbriated extremity resting close to the sacro iliac articulation of the corresponding side. The outer two-thirds of the oviducts show numerous windings; the inner third is nearly straight.

Peritoneal Investment.—The tubes are enclosed within the upper free border of the broad ligament which forms the mesentery of the tube—mesosalpinx. Macroscopically the fimbriated end appears to pierce the posterior surface of the broad ligament about 2 cm. away from the firm attachment of its reflection to the lateral pelvic wall. The broad ligament between the tube and pelvic wall has a sharp crescentic border known as the infundibulopelvic ligament.

Size.—The tubes are usually from 10 to 12 cm. long. Variations in their length of from 6 to 20 cm. have been noted. As a rule the tubes are slightly unequal in length (according to Quain the right is usually the longer).

Divisions.—The tube shows differences in appearance, structure and lumen according to the portion examined. It has, therefore, been divided into three parts which insensibly merge into each other.

The isthmus, or inner third of the tube, about 3 cm. in length and 3 to 4 mm. in diameter, is straight, firm and cord-like. In the first part of its course it lies embedded within the uterine wall (*interstitial* portion).

The ampulla, as the next succeeding portion is called, forms more than one-half of the total length of the tube. It gradually increases in diameter from within outward, is softer to the touch, and tortuous in its course. Its length is about 8 cm., its diameter 6 to 8 mm.

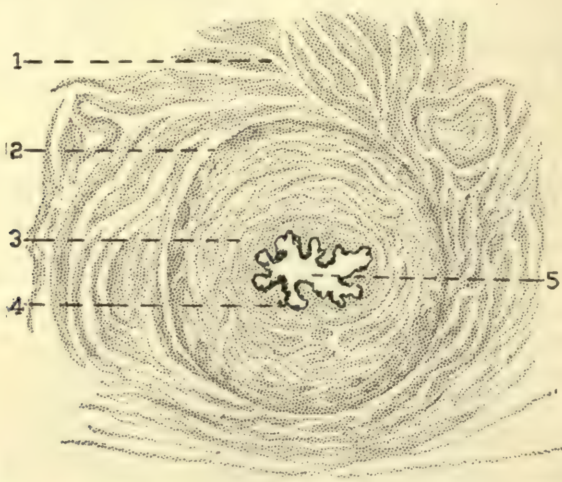


Fig. 26.—Transverse section of fallopian tube: Interstitial part. (×20.) 1. Uterine musculature. 2. Outer limit of tubal wall. 3. Tubal musculature. 4. Tubal epithelium. 5. Tubal lumen showing few and low rugae.

The infundibulum is the trumpet-shaped free termination of the oviduct (fimbriated extremity). Its margin is prolonged by irregular processes, the fimbriae, which vary in shape, size and number. The main fringes average 1 to 1.5 cm. in length. From them arise minor prolongations. One of the fimbria is prolonged along the free border of the mesosalpinx to the ovary,

or if it does not reach this gland, the interval is bridged by a peritoneal prolongation. This *fimbria ovarica* has a longitudinal groove, which represents the nearest approach to continuity between the sex gland and its excretory duct.

Lumen.—The canal begins at its uterine extremity by means of a round, narrow opening (os uterinum) 1 mm. in diameter (Fig. 26). The isthmic portion has a stellate lumen resulting from the formation of mainly longitudinal folds, which continually increase in size and number to the

FIG. 27.—TRANSVERSE SECTION OF FALLOPIAN TUBE: ISTHMIC PART. (×20.) Lumen has increased, folds multiplied. The tubal wall is thick. Below is the mesosalpinx.

infundibular extremity (Fig. 27). In the ampulla the lumen is obscured by complex primary and secondary folds, continuous with those of the infundibulum, and prolonged upon the fimbriae. The line of transition between the mucous membrane covering the fimbriae and the peritoneal coat follows the bases and outer surface of the fringes. The inner opening of the oviduct (ostium abdominale) is 2 mm. in diameter. The isthmic portion of the tube admits a bristle or a fine filiform, the ampullary part a uterine sound.

At birth the tubes are not only shorter, but much more winding than in the adult. Their fimbria are fewer, the folds less in number and lower. *In old age* the oviducts are paler and thinner than during the sexual period.

II. **Normal Histology of the Fallopian Tubes.**—The Adult Tube. —The oviduct on section shows three main layers. The most external is the outer peritoneal investment completely surrounding it except at the base, where the vessels, nerves and lymphatics approach between the folds of the mesosalpinx (Figs. 26–28). The next layer consists of a muscular tunic upon which the innermost coat, the mucous membrane, rests.

Fig. 28.—Transverse section of fallopian tube: Ampullary part. (×20.) Note increase in diameter of lumen and multiplication of folds over Fig. 26 and 27. Blood vessels of mesosalpinx and tubal wall in solid black.

The Serosa is composed of a single layer of flat polygonal cells with oval nuclei, resting upon a thin layer of wide-meshed fibrous tissue containing few cells.

The junction of the peritoneal endothelium with the surface epithelium of the tubal mucous membrane occurs abruptly on the outer surface of the fimbriae near their base.

The Muscle is composed of two strata of unstriped fibers, arranged in an inner circular and outer longitudinal layer. The longitudinal layer is thickest at the upper and lower poles of the oviduct. This layer is best developed in the isthmic portion, and gradually diminishes toward the infundibulum.

The circular musculature also diminishes toward the abdominal end. Many of the smaller bundles run obliquely, interlacing with the more circularly placed fasciculi.

The Mucous Membrane consists of surface epithelium, connective tissue and longitudinal muscle fibers.

The muscle fibers form a compact longitudinal layer immediately beneath the epithelium in the interstitial part of the oviduct. Though in contact with the uterine musculature, the tubal muscle can be readily distinguished. In the outer portion of the isthmus a fine connective tissue

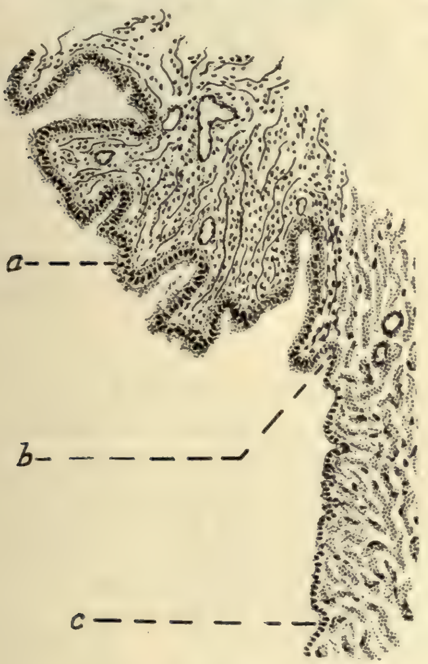


FIG. 29.

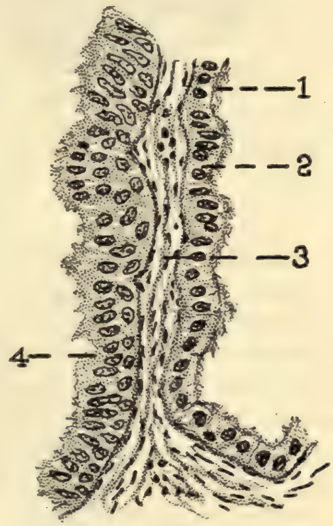


FIG. 30.

FIG. 29.—SECTION OF TUBAL FIMBRIA. (M.P.) Shows junction of tubal and peritoneal epithelium at ostium abdominale. *a*. Epithelium lining tubal fold (columnar ciliated). *b*. Point of junction. *c*. Low peritoneal endothelium.

FIG. 30.—SECTION OF TUBAL FOLD. (H.P.) 1. Ciliary margin. 2. Epithelial cells. 3. Connective tissue frame work. 4. Slanting cut producing seemingly multilayered epithelium.

interposes between the surface epithelium and the longitudinal layer, which becomes progressively thinner and less compact. In the ampulla this inner longitudinal muscle appears only in the form of scattered bundles, and the connective tissue is proportionately increased.

The connective tissue just described, except in the interstitial part of the tube, forms the framework for the tubal folds. It is composed of round and spindle cells, and harbors the vessels and lymphatics which ramify beneath the epithelium of the folds.

The epithelium is usually described as a single layer of columnar ciliated cells, 15 to 20μ high, with an oval nucleus, median in position. Moraller and Hoehl mention that the nuclei of adjacent cells occupy higher and lower levels and that, in consequence, every third or fourth cell appears cubical. The epithelium at the base of a fold is higher than that at its

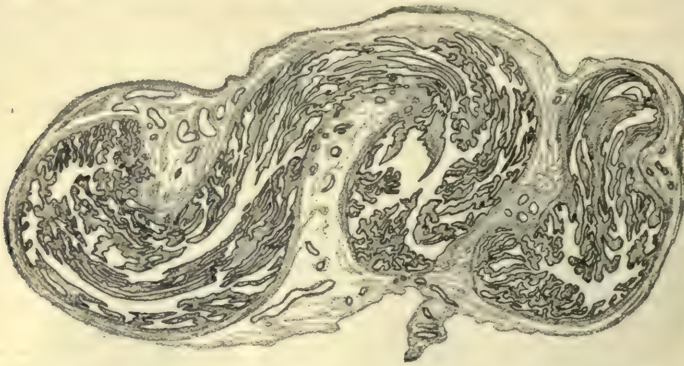


FIG. 31.—LONGITUDINAL SECTION OF TUBE: NEWBORN. (×20.) Owing to tortuosity of infantile tubes the lumen was cut three times in one section. Note multiplicity of folds.

FIG. 32.—TRANSVERSE SECTION OF FALLOPIAN TUBE: Woman 63 years old. (L.P.) Section is at beginning of ampullary portion. Note thick fibrotic muscle layer, simplification of mucosal folds, both due to senile atrophy.

apex. The fimbria ovarica is covered with ciliated epithelium similar to that lining the tube. Scattered islands of ciliated epithelium may be found on the ovary or on adjacent parts of the broad ligament (Gebhard).

The vessels run longitudinally in the longitudinal outer muscle layer, are circularly disposed in the circular layer, and finally run parallel to the direction of the folds of the mucous membrane.

Lymphatics are numerous.

The *nerves* form a subserous plexus, send branches to the muscle, and penetrate to the epithelium (subepithelial end buds).

Elastic fibers in the tube are long and thick. They are most numerous beneath the serosa and about the vessels. The elastic tissue diminishes toward the ampulla.

In the newborn the tube shows more windings because the circular muscle layer is thicker and the longitudinal layer shorter (Winter). The epithelium has no cilia. Elastic fibers are absent.

In old age.—Even before the menopause the connective tissue of the oviduct increases in quantity about the larger vessels and between the muscle bundles (Moraller and Hoehl l. c. 1). This fibrosis is intensified after the menopause. The musculature atrophies. The folds first lose their plump configuration, become angular, more closely packed, and finally, by adhesion of adjacent surfaces may obliterate the lumen. The surface epithelium loses its ciliary margin, and changes from columnar to low cuboidal or even flattened form. The elastic fibers diminish in number.

THE OVARIES

I. **Gross Anatomy in the Adult.**—The ovaries are bilateral, solid organs which are usually classified as ductless glands, but in reality, like the testes, are intermediate between the simpler glands with excretory ducts and ductless glands proper. The excretory duct of the ovary is represented by the fallopian tube, the gap between oviduct and sex gland being bridged by the fimbria ovarica (Fig. 15, p. 27), the ovum representing the secretion. The internal secretory products are derived from the follicular apparatus, especially from the corpus luteum, and possibly also from the interstitial cells. In some animals the connection between ovary and tube is more intimate, a peritoneal pocket enclosing the ovary, and, by means of a funnel-shaped opening, leading directly to the infundibulum. This disposition has been described in the human being in rare instances.

Appearance and Size.—The ovaries are elongated, flattened bodies, roughly almond shaped, but varying greatly in their configuration. The surface is raised by rounded bosses (follicles, corpora lutea), and shows fissures, pits and scars (Fig. 256, p. 368). The color of the organs is grayish-white and less glistening than that of other abdominal organs. Their size is very variable and fluctuates constantly in each individual from puberty to the menopause, but on the whole increasing to the fortieth year. The average length is 2.5 to 5 cm., width 1.5 to 3 cm., thickness 0.6 to 1.5 cm. The weight ranges between 5 and 7 gms.

For purposes of anatomical description a median and lateral surface are given. The anterior margin is straight and is attached to the posterior surface of the broad ligament by means of the short mesovarium (region of

the hilum). A white, somewhat irregular line parallel to the long axis of the ovary marks the change from the glistening peritoneal endothelium to the lusterless ovarian surface epithelium and corresponds to the hilum. Approximately one-third of the ovary projects within the mesovarium, anterior to the white line. The posterior margin is convex, rounded, and projects free into the peritoneal cavity. The upper or tubal pole is blunt; the lower, uterine is pointed.

Position.—The position is variable, depending mainly upon the position of the uterus. When this organ is anteflexed the ovaries lie nearly vertically placed against the lateral pelvic wall just below the brim, and extend downward toward the uterus but behind it. The lateral surface of the ovary then rests in a peritoneal depression, the fossa ovarica, described by Waldeyer as an equilateral triangle formed by the round ligament as its base, the external iliac vein as its upper and the ureter as its lower leg. The position varies within wide limits, depending upon the changes in the position of the uterus, the pelvic contents, and the tightness of its ligamentary support. The upper pole of the ovary is hidden by the ampullary portion of the fallopian tube which curves across it.

The ovarian ligaments are three in number. *The suspensory ligament* (infundibulopelvic) formed by the free crescentic border of the broad ligament, is responsible for the vertical position of the ovary. This triangular band, covered by peritoneum, and of varying length, attaches to the upper pole and is composed of fibromuscular tissue, supporting the ovarian vessels and nerves. The fimbria ovarica courses along its free edge. *The utero-ovarian ligament* (ligamentum proprium) appears as a rounded cord covered by the peritoneum, connecting the lower pole with the cornu of the uterus. It is 2 to 3 cm. long, and 3 to 4 mm. thick.

The mesovarium, which is a short fold (2 to 5 mm.) derived from the posterior surface of the broad ligament, ends abruptly at the white line. Between the folds of the mesovarium the ovarian vessels, nerves and lymphatics enter and leave the ovary.

Structure.—Transverse section of the gland shows two main zones, an outer thin *cortical* (parenchymatous), which extends over the entire periphery except at its hilum, and an inner *medullary* (vascular) embraced by the cortex (Fig. 34).

The cortex is 2 to 3 mm. thick. In the cortical zone may be seen smaller and larger thin-walled cystic cavities (1 to 1.5 cm.) which project outward from the medulla, and may form bosses on the surface of the ovary. These are ripening or ripe graafian follicles.

The earliest stages of corpus luteum formation are usually not recognized. According to R. Meyer small, flabby, ruptured vesicles, without blood clot in their interior often prove to be the first stage of the yellow body upon microscopic examination. More advanced corpora lutea appear as larger, bluish to red nodules which, when cut across, show their center occupied by fresh or organizing blood clot, the walls supporting a wavy,

yellow membrane, which projects inward to form convoluted folds. A corpus luteum may occupy as much as one-third of the entire ovary. At a later stage these bodies lose their red and yellow coloring and appear fibrous, but continue to show the same gross structural relations for long periods (corpora albicantia) (Fig. 33).

Small cysts similar to graafian follicles, but characterized by greater vascularity (appearing bright red in the fresh state especially when on the surface), and having a thicker wall, are atretic follicles. Macroscopic differentiation between ripening and atretic follicles is usually impossible.

The medulla shows as a paler fibrous tissue containing large and convoluted blood vessels.

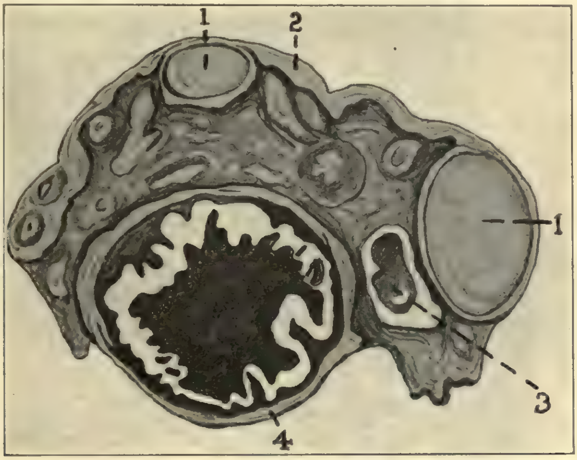


FIG. 33.—CUT SURFACE OF OVARY (SPLIT OPEN). (×2.) Removed four days before menstruation. 1. Cystic atretic follicle. 2. Thickened albuginea. 3. Cystic corpus albicans. 4. Fresh corpus luteum with crenated lutein layer and fresh blood clot.

At birth the ovaries are smaller than in the adult, but proportionately longer and narrower (1.5 cm. long, 0.5 thick). The sex glands lie above the brim of the pelvis into which they descend by the second year. They are more pinkish because the albuginea is thinner and translucent. Their shape is prismatic and their surface unfurrowed and devoid of scars. On section cystic follicles are sometimes noted (Prochownick, Arch. Gynäk. 1881, XVII, 330).

After the menopause the ovaries are smaller, often deeply fissured and scarred. On section they are found hard and fibrous. Cystic follicles and corpora albicantia may persist to extreme age.

II. **Normal Histology of the Ovary.**—THE ADULT OVARY.—The following layers are distinguished from without inward: (*a*) the surface epithelium; (*b*) a poorly defined connective tissue capsule, the tunica albuginea; (*c*) the parenchyma or cortex which harbors the ova; (*d*) the medulla, containing the blood vessels, nerves and lymphatics, and certain

fetal remains known as Köllicker's medullary cords and the tubules of the rete ovarii (Figs. 34 and 35).

(*a*) *The Surface Epithelium* (formerly called the germinal epithelium) consists of a single layer of low cuboidal cells, which covers the entire surface of the ovary to the hilum where there is an abrupt transition to the low peritoneal endothelium (white line). The cells dip down into all incisures and furrows, which they, likewise, line. In these depressions the cells are

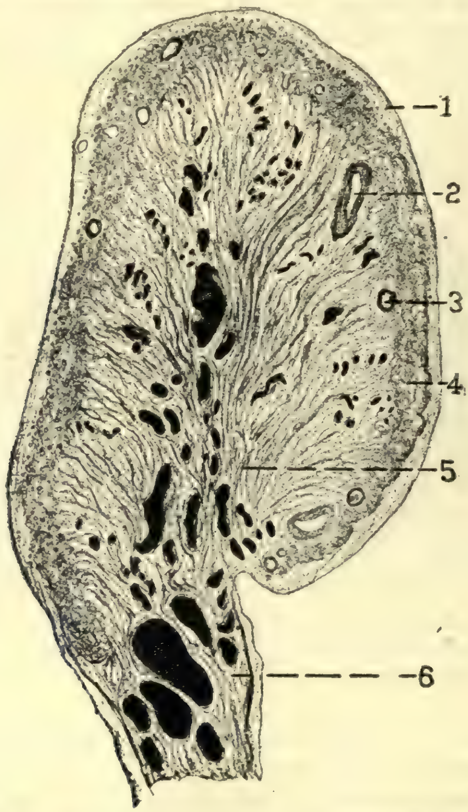


FIG. 34.—TRANSVERSE SECTION OF ADULT OVARY. (×5.) 1. Tunica albuginea. 2. Large atretic follicle. 3. Ripening graafian follicle. 4. Parenchyma or cortex containing primordial follicles. 5. Medulla. 6. Hilus, showing ovarian vessels (solid black) entering through mesovarium.

higher than at the surface. The nucleus of each cell is oval and sharply outlined. The cell protoplasm is granular. (See Fig. 271, p. 396).

(*b*) *The Stroma,* immediately beneath the surface epithelium, forms an ill-defined layer of interlacing fibers, 0.5 to 1 mm. in thickness, which is known as the *tunica albuginea.* In the parenchymatous zone the connective tissue is very cellular, consisting chiefly of spindle cells, which, except where they run in well-defined bundles about the ovular elements and merge with their outer tunic, show no definite arrangement. In the medulla the con-

nective tissue is less dense, less cellular and more wavy. It forms the support for the vessels, nerves and lymphatics. In the outer zone elastic fibers are numerous; in the medulla they are found chiefly in the neighborhood of the vessels. Scattered unstriped muscle fibers are found particularly in the medullary zone, or arising below the surface epithelium, radiate from the hilum to the cortical zone.

(*c*) *The Parenchymal Layer—Ova and Their Derivatives.*—In order to describe the parenchyma of the ovary it will be necessary to refer constantly to follicles and ova in various stages of development. Therefore it is preferable to describe these bodies before detailing their distribution and relations.

The histology of the ova, their growth and evolution is one of the most difficult chapters in anatomy, because even to-day, after more than 80 years

FIG. 35.—HORIZONTAL SECTION THROUGH BROAD LIGAMENT OF NEWBORN SHOWING TOPOGRAPHY. (×10.) 1. Transverse sections of fallopian tube. 2. Ovarian parenchyma with many primordial follicles. 3. Surface epithelium of ovary. 4. Corpus atreticum of large size. 5. Tubules of epoöphron (wollfian remains) in mesovarium. 6. Ovarian vessels (solid black) entering the hilus.

of study (v. Baer discovered the human ovum in 1827) no unanimity has been reached concerning many details. In order to understand the development of the various forms encountered in the adult, it will be necessary to trace the ovum from its earliest stage in the fetus, and follow its development and evolution in infancy and through puberty. The confusion has arisen mainly because the ovum is not a stabile unchanging structure, but one constantly undergoing growth and involution. Therefore, it is necessary to study these structures at each stage while keeping the preceding and succeeding steps in mind.

The forms to be considered are:

1. Primitive ova, Pflüger's tubes, egg nests.
2. Primordial follicles.
3. Graafian follicles—small, ripening, ripe, ruptured (ovulation).
4. Corpus luteum formation, corpora albicantia.
5. Atresia.

1. DERIVATION.—In the germinal (surface) epithelium covering the median ventral portion of the wolffian body large cells are found—the primitive ova (10 to 16μ, nucleus 8μ). Invasion of the mesoderm subdivides the epithelial masses in which these cells lie into smaller aggregations which in many instances retain their continuity with the surface epithelium producing transitory rodlike columns called *Pflüger's tubes*. By further isolation of the cell masses single large cells, surrounded by a layer of germinal epithelium result, the so-called primordial follicles, which form the starting point, in infancy and adult age for all further evolutions of the ovum. These develop in the fifth month of intra-uterine life.

2. THE PRIMORDIAL FOLLICLE consists of one (rarely two or more) large cell enveloped by a layer of low endothelial-like cells, which have no distinctive membrana propria separating them from the stroma. *The ovum* is elliptical, 54 to 58μ in size when examined in the fresh state (Nagel (10)) and contains a large nucleus (29 to 32μ) demarcated by a doubly refractive membrane. The nucleus contains a nucleolus, paranucleolus, and a chromatin network. The protoplasm is finely reticular (Fig. 36).

FIG. 36.—TWO PRIMORDIAL FOLLICLES FROM OVARY OF ADULT. (H.P.) Central in each follicle is the ovum, with nucleus and nucleolus. A few follicle cells (these later become granulosa cells) line the cavity. The ovarian stroma surrounds the follicle.

The outer epithelium is flat, like endothelium. Each cell has an oval or elongated nucleus. These cells lie in close contact with the ovum.

Fate of the Primordial Follicle.—Nagel (l. c. 10) believes that primordial follicles remain unchanged until the menopause, unless they, on the one hand, develop into graafian follicles, or, on the other hand, undergo atresia and disappear. Schottlaender (11), however, claims that such primordial follicles as persist, enlarge progressively from infancy to puberty, and then either develop or undergo atretic changes. It is certain that an enormous number of primordial follicles, which Waldeyer estimated as 100,000 at

birth, and Henle as 36,000 at puberty, disappear before puberty by the process of atresia.

Atresia of primordial follicles is initiated by the disintegration of the ovum, the enveloping cells then disappearing. The surrounding stroma fills up the gap without any scar formation (Palladino, 12).

3. GRAAFIAN FOLLICLES develop in a few instances even during intra-uterine life. In infancy and childhood a small number form, but do not attain full development (Benthin (13)). During the period of sexual activity they grow in large numbers, and at the onset of the menopause the few remaining ova may continue to develop for a short and variable period.

FIG. 37.—RIPENING GRAAFIAN FOLLICLE. (H.P.) The ovum has enlarged, the granulosa cells have multiplied, internal theca cells are distinguishable; no follicle cavity has formed. 1. Nucleolus of ovum. 2. Cytoplasm of ovum. 3. Granulosa cells. 4. Zona pellucida. 5. Theca externa. 6. Neighboring primordial follicle. 7. Theca interna.

Development of the Graafian Follicle.—The narrow, endothelial-like enveloping cells assume cubical and cylindrical form, multiply by mitotic division, and become stratified (membrana granulosa) (Fig. 37, 3). The surrounding stroma, likewise, undergoes changes by the time the granulosa cells have multiplied to more than three rows of thickness. The layer immediately adjacent to the granulosa cells differentiates into a fine felt-work of fibrils between which lie round and polygonal cells. This area is called the *theca interna;* the larger polygonal cells which early take up fat are known as *theca lutein cells.* The theca (wall) harbors a constantly increasing capillary network. Surrounding the theca interna is a concentric layer of interlacing small spindle cells (theca externa), differing but little

from the ovarian stroma, but surrounded by a closely interwoven net of capillaries which form an almost cavernous tissue.

Some of the granulosa cells undergo vacuolation, liquefaction and disappear. Simultaneously by osmosis from the capillaries in the theca interna, fluid enters the cavity which thus results. The cavity is first sickle, then halfmoon shaped, and constantly enlarges. The separation takes place within the layers of the granulosa cells, so that not only does the ovum remain encircled by a layer of these cells, but the external boundary of the *follicular cavity* is also formed by them. At this stage the separation between granulosa cells and theca interna is more sharply emphasized by the formation of a homogeneous membrane, the *glass membrane*.

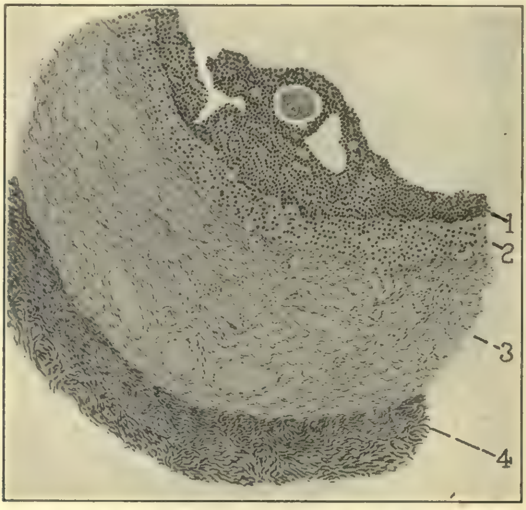


FIG. 38.—REGION OF THE OVUM IN A MATURE GRAAFIAN FOLLICLE. (H.P.) Drawn to smaller scale than Figs. 36 and 37. 1. Granulosa layer containing ovum on its discus proligerus. 2. Theca interna. 3. Theca externa. 4. Ovarian stroma. Above is follicle cavity.

The ovum lies eccentrically situated, surrounded by a mantle of cells (corona radiata) upon the apex of a mound of granulosa cells, known as the *discus proligerus* or *cumulus oophorus*. Thus the ovum, protected by its mantle, projects into the follicular cavity. Usually the point of attachment (discus proligerus) is situated directly opposite to that portion of the follicle wall which is nearest to the surface of the ovary (Fig. 38).

The cells of the corona radiata, and the outermost layer of granulosa cells are cylindrical. The deeper layers of the granulosa are irregularly polyhedral and are prolonged into protoplasmic processes.

Changes in the Ovum.—Meanwhile a membrane, in which under highest magnification, radial striations can be distinguished, has surrounded the ovum (*zona pellucida*). Internal to this a capillary space, the *perivitelline space*, is described, though it is doubtful whether this exists in the fresh state. The protoplasm of the ovum shows two distinct zones, a clear

peripheral region, and a central granular area which surrounds the nucleus. The granules represent the vestiges of the yolk or deutoplasm, which is so well developed in certain lower species. The oval nucleus, excentrically placed at the upper pole, has a doubly refracting nuclear membrane and contains a nucleolus and paranucleolus (Fig. 37).

This stage of ripeness is noted not only in infancy but also in the newborn. Before puberty, however, the ova which attain this stage of development do not progress further, but undergo regressive changes (atresia), to be described below. The great majority of ova in infancy and childhood begin to regress before the granulosa cells have multiplied largely and before a distinct follicular cavity has had time to develop. According to Straatz 1500 ova attain this degree of development. Strassmann (14) regards this estimate as too high.

Complete Maturation, Follicle Rupture *(Ovulation)*.—Further changes that take place occur chiefly within the nucleus of the ovum. These changes have never been observed in the human being and can be studied only in animals (see books on embryology). As long as a well-marked nucleus is present the ovum is not ready for fecundation.

Before extrusion of the ovum from the follicle, the cells of the discus proligerus undergo fatty degeneration, which serves to weaken the connection between ovum and follicular wall. The follicle has reached dimensions of 1 to 1.5 cm., is tense, and protrudes above the ovarian surface. At the future site of rupture (the stigma) the covering layers become thinned and blanched. Surrounding this area is a radial aggregation of vessels.

The ripe ovum, which is the largest cell in the body, measures 200μ including its zona pellucida, the nucleus 40 to 50μ, the nucleolus 5 to 7μ, the zona pellucida 10μ (Waldeyer (l. c. 1)). The ovum is just visible to the naked eye. With follicular rupture the act of ovulation has occurred. The further fate of the ovum does not concern us here. The changes in the ruptured follicle fall under the heading of:

4. Corpus Luteum Formation.—The earliest stages of the corpus luteum until recently have been overlooked in the human being, attention having been focused upon the hemorrhagic stage and later development. This was largely due to the fact that the recently ruptured follicle consists of an inconspicuous flaccid and collapsed vesicle, which does not resemble the later formation (Figs. 39–44). Robert Meyer (15) has described the early stage and demonstrated that the process in the human species closely approximates that so carefully studied in the mouse and rabbit by Sobotta. Meyer's description is the basis of what follows.

The distinction between the *corpus luteum of menstruation* (so-called corpus luteum spurium) and of *pregnancy* (c. l. verum) consists mainly in the size, degree of development and persistence of the yellow body. If impregnation fails to take place, the corpus luteum does not exceed the dimensions of the follicle and rapidly regresses; if conception occurs, the corpus luteum increases up to the third or fourth month, and may reach a

size of 2.5 to 3 cm. in its largest diameter (Fig. 39). It usually persists into the puerperium (25 days post partum according to Miller (16)). Differences in minute structure, such as have been described by some authors, will be referred to later.

Proliferative Stage.—In the flaccid ruptured follicle the granulosa (epithelial) cells show marked mitotic activity, increase rapidly in number and form an increasingly deep layer lining the cavity (Figs. 40 and 44). Individual cells increase in size, plumpness and irregularity of contour (lipoid and fat absorption). The theca interna (connective tissue) cells are more conspicuous at this stage than the granulosa cells, because, even before the extrusion of the ovum, they contain fat and surround the follicle proper as a sharply demarcated broad and continuous belt (theca lutein cells) (Fig. 40). The separation between external and internal theca is not well defined.

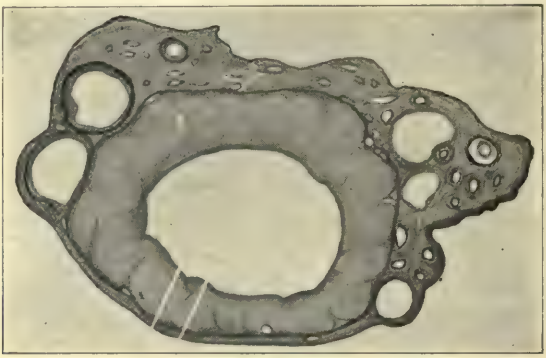
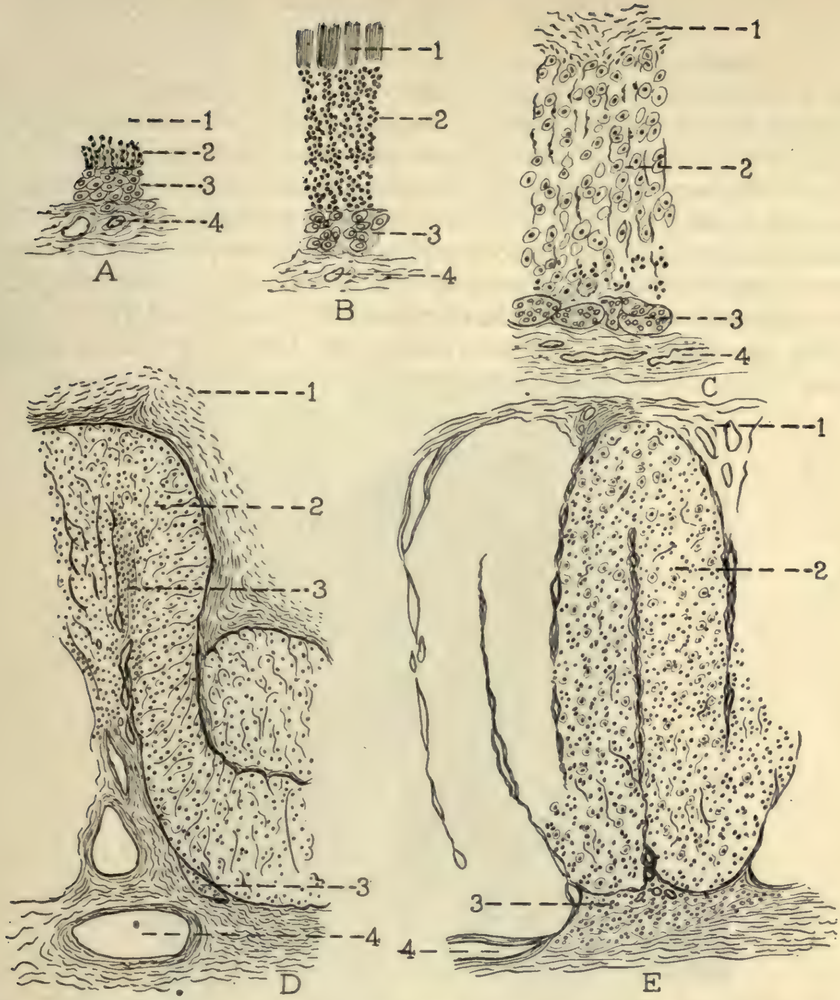


FIG. 39.—CYSTIC CORPUS LUTEUM (PREGNANCY). (×2.) Note large size of yellow body, its cystic central cavity and thick yellow (lutein wall), also the many atretic follicles in the ovarian stroma. For high power of portion between parallel lines see Fig. 48, p. 59.

A constantly increasing capillary network develops in both thecal layers and penetrates to the granulosa (Fig. 41B).

Glandular Stage.—The progressive increase in size and number of the granulosa cells produces a wavy contour toward the follicular cavity, which has again become a closed sac. The capillaries which have penetrated to the granulosa form hernial projections between its cells, rupture, and pour blood into the follicular cavity, where liquor folliculi, blood cells and fibrin, by coagulation, produce a pale red, jelly-like mass, which, as more blood is effused and as solidification increases, results in the red central core, considered characteristic of the corpus luteum. This effusion into the central cavity is, however, secondary and neither indispensable nor invariably associated with the formation of the yellow body. Meanwhile the capillaries continue to proliferate, form dilated winding and angular channels between the granulosa cells and, after penetrating this layer, enter the follicle cavity, spread out upon the inner surface of the granulosa cells and begin to invade the central coagulum as well. (*Vascular stage,* Figs. 42 and 47.) With the



FIGS. 40–44.—FORMATION OF THE CORPUS LUTEUM (SCHEMATIC). Cross sections of part of wall of corpus luteum at different stages. In all 1. is follicle cavity. 2. Granulosa cells (in Figs. 40 and 41), lutein cells in later figures. 3. Theca lutein cells (connective tissue origin). 4. Theca externa.

FIG. 40A.—WALL OF RECENTLY RUPTURED MATURE GRAAFIAN FOLLICLE: Cavity (1) either empty or filled with blood. Theca lutein cells (3) prominent.

FIG. 41B.—PROLIFERATIVE STAGE: Follicle cavity (1) filled with gelatinous clot, granulosa cell layer thick, but containing no lutein and no blood vessels.

FIG. 42C.—VASCULARIZATION STAGE: Follicle cavity lined and filled with connective tissue (replacing central clot), granulosa cells changed to lutein cells with narrow blood capillaries between cells. Theca lutein cells (3) less prominent.

FIG. 43D.—RIPE STAGE (functional activity): Follicle cavity completely shut off by connective tissue (1), lutein layer now thick, crenated and containing much lipoid, many vessels (2); theca lutein cells, small in number and relegated to the septa (3).

FIG. 44E.—THIRD MONTH OF PREGNANCY: Well-defined gland resembling the adrenal cortex in structure.

increased blood supply the granulosa cells rapidly absorb more fat, and assume the full, yellowish, granular and poorly staining aspect characteristic of *lutein cells.* A small amount of connective tissue, from the theca interna, in the form of young spindle cells and numerous fibrils, now grows along the paths of the capillaries, rapidly increases to form thin septa between the lutein (changed granulosa) cells and penetrates to the central core. Once established in the centrum, the connective tissue grows along the surface of the epithelium (lutein cells) sending strands centrally into the coagulum, and peripherally outward into the epithelium (Figs. 43D and 47).

The new capillaries and their contents, the increasing amount of connective tissue, and the hypertrophy of the granulosa (lutein) cells all serve

FIG. 45.—WALL OF RECENTLY RUPTURED FOLLICLE. Photomicrograph. (H.P.) Note feathery margin of granulosa cells (1) bordering on the follicle cavity. (2) and (3) shows thick layer of theca lutein cells, below this the theca externa.

to enlarge the follicular cavity, and to produce pressure upon the walls (theca). In response to this expansile impulse, particularly at such spots at which counter-pressure is exerted externally by adjacent large unruptured follicles or corpora albicantia, the theca interna is thinned out irregularly and its large lutein-like cells (theca lutein) crowded apart into small groups (Figs. 43 and 44).

This process continues for a variable period, during which the lutein cells become more prominent, the theca cells less and less discernible.

The ripe corpus luteum has a broad, ruff-like, very wavy, yellow margin surrounding the central core, which gradually becomes paler and firmer. The lutein cells stain equally, are pale, plump and clear. The capillaries run straight, more or less radially and are now narrow. Firm septa interdigitate

from within the core, with those penetrating externally from the theca. The theca lutein cells are fewer, scattered and best preserved in the septa where they are protected from pressure (Figs. 43 and 44).

Regressive Stage.—The core becomes irregular or contracted; it may become cystic or harbor a hematoma. The lutein cells are vacuolated, unequal in their staining qualities, and finally lose all power to accept stains. Empty spaces, formerly occupied by lutein cells, abound (Fig. 48). The connective tissue becomes increasingly hyaline, and the vessels show corresponding hyaline changes. Theca lutein cells have disappeared. When

FIG. 46.—LATE PROLIFERATIVE STAGE OF CORPUS LUTEUM, BEFORE VASCULARIZATION. Photomicrograph. (H.P.) For details see Fig. 42.

progressive atrophy of all the elements has taken place as evinced by the continued shrinkage, gradual transformation of all the parts into hyaline matter, and a general appearance of homogeneousness, the remains of the corpus luteum are known as the *corpus fibrosum* or *albicans*. The vessels of the theca externa are involved last of all. At first they merely contract, later their adventitia and finally their musculature becomes hyaline, and eventually the endothelium desquamates with consequent obliteration of the lumen. The distorted corpus albicans persists for a long time in the form of a homogeneous mass of very varied shape (cork-screw, half moon, sickle, star or leaf shaped).

The above is an attempt to present a panoramic view of the changes observed in the development, glandular stage and ultimate obliteration of

the yellow body. Certain minuter details of cellular structure and certain distinguishing features between the corpus luteum of menstruation and pregnancy also require mention.

The granulosa lutein cells of the corpus luteum of menstruation are 10 to 12μ in size; those of the corpus luteum of pregnancy 20 to 60μ. The cells are polygonal, contain a cloudy, finely granular protoplasm with many fat droplets and some yellow pigment (lipochrome). The nucleus is large and oval. The stroma is formed by pale spindle cells in a wide-meshed fibrillar network. The entire lutein layer with its rows of large, pale cells

FIG. 47.—EARLY RIPE STAGE OF CORPUS LUTEUM AFTER VASCULARIZATION. Photomicrograph. (H.P.) See Fig. 43.

abutting on both sides against thin-walled capillaries, closely resembles the structure of the adrenal gland (Fig. 44).

Miller (l. c. 16), in particular, distinguishes sharply between the products of epithelial (granulosa-lutein) degeneration—*colloid,* and of connective tissue degeneration (theca)—*hyaline,* by means of microchemical reactions. In the corpus luteum of menstruation the sole degeneration is hyaline from the theca cells. In the corpus luteum of pregnancy, after the fifth month, he finds colloid in the lutein areas, also mulberry-like lime deposits of small size (size of lutein cells) and hyaline degeneration of the stroma.

The description of the corpus luteum has been given in such detail because, until recently, no approach to unanimity could be found in the

literature. Any attempt to study such vital problems as the relation of ovulation and corpus luteum formation to menstruation, fertility and uterine disturbances of ovarian origin presupposes a thorough knowledge of these details. Only by the coöperation of clinician and pathologist may we hope to increase our knowledge in this field (see Chapter IV).

5. Follicle Atresia.—The arrest of development, regression and obliteration of an ovum and its unopened follicle is known as atresia. As previously mentioned, by far the greater majority of ova fail to reach

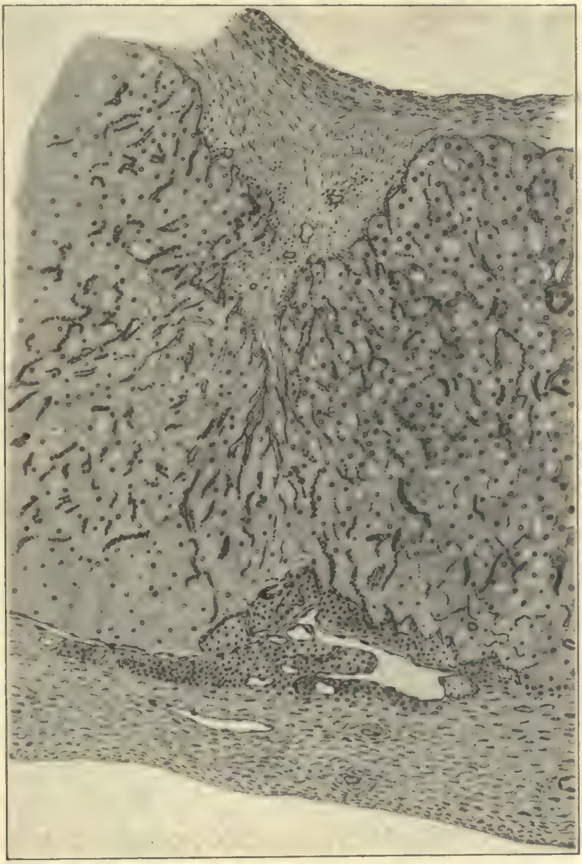


Fig. 48.—Cystic corpus luteum of pregnancy. (High power of Fig. 39, p. 54.) Note vacuolation of lutein cells. Surface epithelium of ovary at lower margin.

maturity, their envelope does not burst and they perish by atresia at various stages of development. The simple process which brings about these changes in the primordial follicle and in the very young ripening follicle (before the granulosa has multiplied or a follicular cavity has been formed) has been described. Atresia, setting in at a more advanced stage of ripening, is more complicated, and is readily confused with normal ripening and with corpus luteum formation—hence much unnecessary obscurity has arisen.

Types of Atresia.—In the main there are two types, the *obliterative* which affects chiefly small and moderate-sized follicles, and the *cystic,* by means of which larger follicles are absorbed. These differences are largely accidental.

Intrafollicular changes are alike in both forms. The nucleus of the ovum undergoes chromatolysis. The protoplasm becomes fatty and albuminous, and fluidifaction supervenes. The granulosa cells, which are undergoing similar changes, at this stage invade the remains of the ovum through the softened and wavy membrana pellucida. The degenerated cell

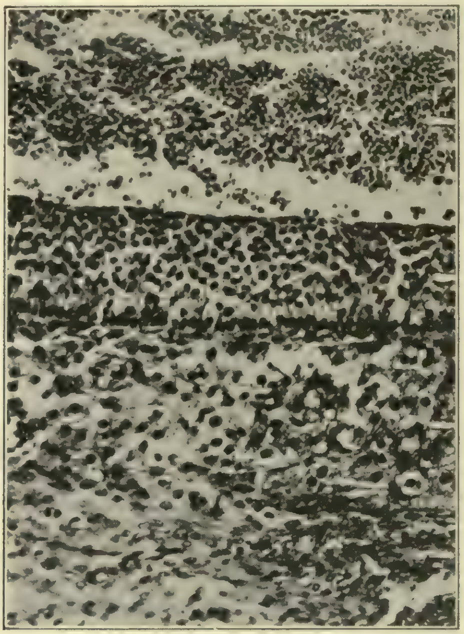


FIG. 49.—WALL OF ATRETIC FOLLICLE. Photomicrograph. (H.P.) From above downward. Follicle cavity containing detritus. Granulosa, note absence of feather edge (see Fig. 45). Theca interna. Theca externa.

masses and the liquor folliculi are absorbed; consequently the follicle collapses.

Thecal changes occur simultaneously with the destruction of the epithelium. The entire connective tissue frame-work is accentuated by multiplication and coarsening of the fibrillar net work, which surrounds almost each individual connective tissue cell. At the junction of the degenerating granulosa and the theca a broad band of fibrils is first noted. This band becomes constantly broader and more homogeneous, as do the other fibrils. Many small capillaries are found. The connective tissue now invades the collapsed follicle cavity through gaps in the homogeneous band, and completes the obliteration by eventually substituting a loose, wavy fibrillar connective tissue with spindle cells, which in the course of time approaches more and more in type to the normal ovarian stroma.

Large follicles undergo cystic atresia, in which the cavity persists for a long time (Fig. 51). Eventually invasion by the thecal connective tissue also takes place. Occasionally follicles collapse early and no connective tissue core develops. These forms

Fig. 50.—More advanced atresia. Photomicrograph. (M.P.) The follicle cavity has been almost completely obliterated by a fine fibrillar connective tissue. The granulosa layer has disappeared, the theca interna (T.I.) and theca externa (T.E.) are hyperplastic. *F.C.* = follicle cavity.

produce rosette-like figures in which the homogeneous band is the most striking structure (corpora candicantia) (Fig. 52).

During pregnancy the atretic process is particularly accentuated. By the end of the sixth month all but the smaller graafian and the primordial follicles have been obliterated.

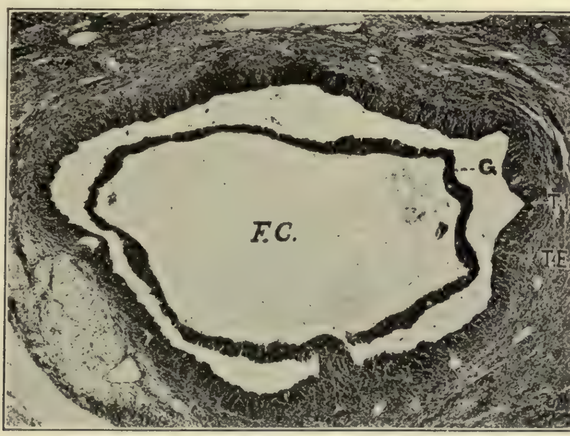


Fig. 51.—Cystic atresia: Early stage. Photomicrograph. (M.P.) Transverse section across atretic follicle. During fixation the granulosa layer (G) has shrunken away from the theca interna (T.I.). Follicle cavity (F.C.).

The atresia in pregnancy differs from that noted at other times in that the theca interna cells hypertrophy and contain much fat and lutein (?) (forming theca lutein cells to an even more marked degree than in the evolution of the corpus luteum) (Seitz (17)). Groups of theca lutein cells are often noted detached and scattered in the ovarian stroma

(Fig. 53). They have been compared to the *interstitial gland* (see Chapter IV), which appears as a well marked structure in certain animals.

Summary.—In the preceding paragraphs the genesis and evolution of the ovum and its follicle has been traced. The process is varied and differs largely with the destiny of the individual egg cell. Of the comparatively few ova to whom it falls to ripen and to be expelled from the ovary (at the most 400), only 3 or 4, or in exceptional instances 10 to 20, become fertilized. The follicles of unfertilized ova, which have been expelled, form the transient corpora lutea of menstruation, the follicles of fertilized ova produce the more persistent corpora lutea of pregnancy. Compared to the ova which partially or completely fulfill their destiny, the number which

FIG. 52.—ADVANCED ATRESIA. Photomicrograph. (H.P.) The follicle cavity is obliterated. Shrinking has given the hyaline band bizarre form. The theca interna (T.I.) cells are resuming a spindle form and the outline of the follicle is no longer definable.

perish as primordial follicles or become atretic at a later stage are enormous (36,000 to 100,000). The physiological importance of these various processes will be discussed in the succeeding chapter.

Distribution of Ova in the Ovary.—Primordial ova in large number occupy the entire parenchymal layer, separated by a variable amount of stroma Fig. 34, p. 48). As the follicles enlarge, and develop into graafian follicles of small or medium size mechanical factors (of pressure) force them inward toward the medulla of the ovary. With further increase in dimensions the enlarging follicles bulge outward through the parenchymal zone, pushing the albuginea before them, and eventually protrude above the surface of the ovary (Fig. 39, p. 54). As a general rule, therefore, primordial follicles occupy the parenchymal zone, small and medium-sized graafian follicles lie beneath the parenchyma, and larger follicles extend from the medulla through all the superficial layers, and finally protrude

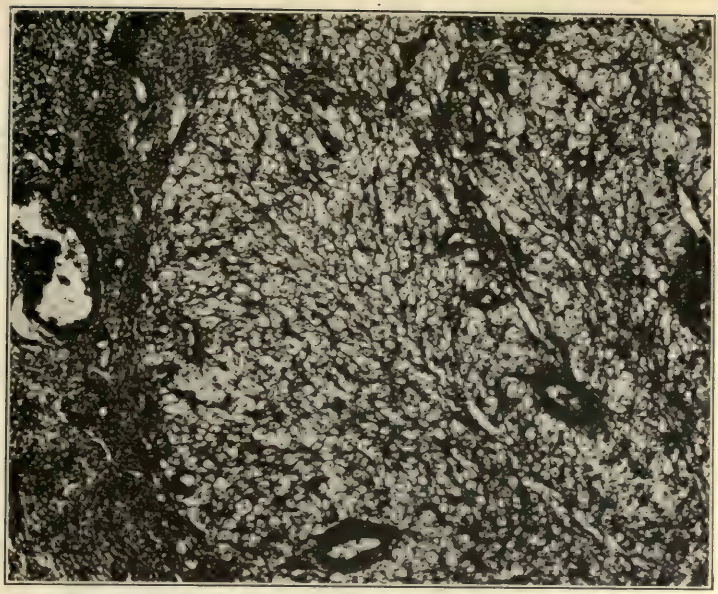


FIG. 53.—INTERSTITIAL GLAND (?) IN HUMAN OVARY. Photomicrograph. (H.P.) Virgin of 23, dysmenorrhea and fibroids. The stroma is formed by fine connective tissue septa enclosing innumerable clear lipoidal cells in their meshes. These areas were widespread throughout the ovary and apparently unconnected with any corpus luteum. Serial section might have demonstrated direct relationship to the corpus luteum.

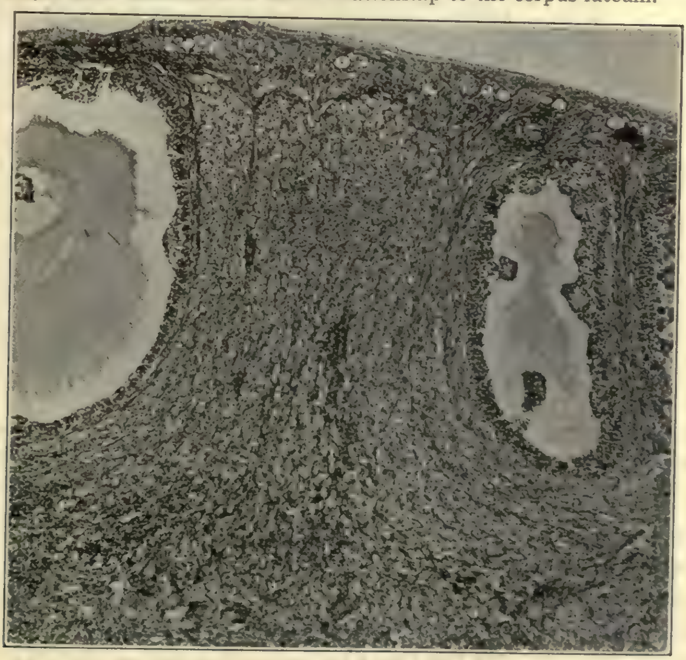


FIG. 54.—INTERSTITIAL GLAND OF A RABBIT. Photomicrograph. (H.P.) The ovarian stroma between the large follicles is composed mainly of interstitial cells. This is normally so in rodents during the sex season and in pregnancy. Compare with Fig. 53.

above the general surface. The same distribution applies to atretic follicles, their position depending upon their size at the time the regressive changes attack them. Corpora lutea at first extend downward from the surface. As they regress and change into corpora albicantia they may lie in the deeper layers.

(*d*) *The Medulla.*—The framework is composed of loose, wavy connective tissue with few spindle cells and some unstriped muscle fibers. A

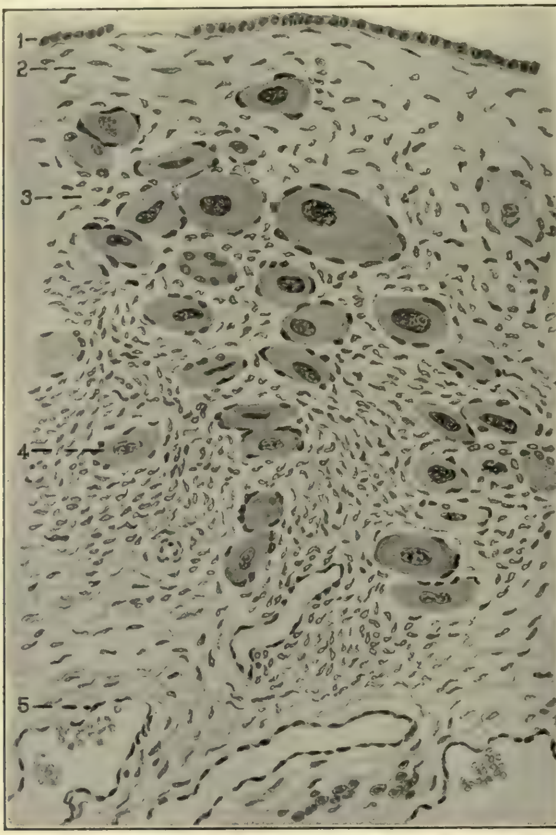


FIG. 55.—OVARY OF NEWBORN. (H.P.) 1. Surface epithelium (high cuboidal). 2. Tunica albuginea (poorly defined). 3. Area of primordial follicles radially arranged. 4. Primordial follicle. 5. Blood vessels.

moderate amount of elastic tissue accompanies the blood vessels. The vessels consist of 6 to 8 large corkscrew arteries, entering at the hilum and extending toward the parenchyma (Fig. 34, p. 48), where they form arches, and send numerous branches which form a close network in this zone. Coarse capillaries invade the theca externa of graafian follicles, and send a finer capillary network into the theca interna.

Many unmedullated nerve fibers enter at the hilum, accompany the vessels, and can be readily traced into the theca folliculi. Their ultimate

distribution is doubtful. Ganglia have been described, and chromaphine cells have been reported by Bucura.

Lymphatic vessels are numerous, emptying eventually into the lumbar glands (Kroemer). The lymph channels in the main follow the spermatic vessels.

AT BIRTH AND IN INFANCY (Fig. 35, p. 49, and Fig. 55) the surface epithelium is higher and more cylindrical than in the adult. The parenchymal zone contains innumerable, closely crowded primordial follicles which reach almost to the surface, because the tunica albuginea is only slightly developed. Near the surface the primordial follicles show some tendency to radial arrangement; as these columns are traced downward toward the medulla, the follicles lie less closely packed and more isolated. Even at birth graafian follicles of varying size are found. They are few in

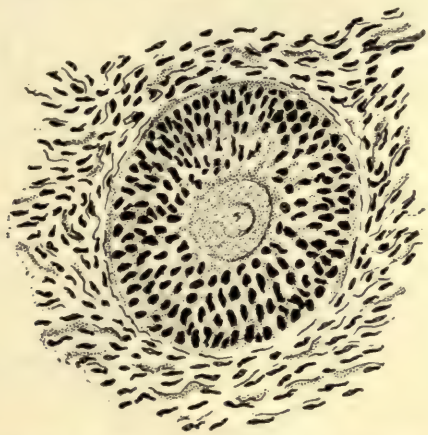


FIG. 56.—GRAAFIAN FOLLICLE FROM OVARY OF WOMAN AGED 62; TWELVE YEARS AFTER ONSET OF THE MENOPAUSE. (H.P.) The ovum and granulosa layer appear perfectly normal. The theca interna cells barely show. The stroma is fibrous.

number at this period in life, but increase during infancy, and become numerous at the approach of puberty. The stroma is less firm and cellular than in the adult. Elastic fibers are found only with the large blood vessels.

After the menopause follicles are usually entirely absent (Fig. 56). The stroma of the ovary is dense and fibrillar. Corpora albicantia and candicantia may persist for years. The blood vessels show senile changes (endarteritis obliterans) and the surrounding connective tissue may form homogeneous bands indistinguishable from corpora albicantia (Moraller and Hoehl).

EMBRYONAL RESTS, though inconspicuous, may, when diseased, play an important rôle (see Parovarium, Chap. XI, p. 000). It is necessary to know their distribution and appearance.

Medullary rays are homologues of the vasa recte in the male. They are found as epithelial strands in the parenchyma. or may form ova and

follicles, or aggregates of cells resembling the alveoli of solid carcinoma. Frequently they appear as mere dense strands resembling connective tissue. The rays are not found in adults (Meyer, R., in Moraller and Hoehl, l. c. l., p. 88).

Rete ovarii are homologues of the rete testis. Peripherally they communicate with the rays, centrally with the epoöphoron. They are found in the hilus of the ovary and may persist in the adult. The appearance is that of net-like, intercommunicating, epithelial-lined clefts, or solid cords without a lumen. The epithelium is irregularly cuboid or low cylindrical.

The Epoöphoron (*Parovarium*) lies at the hilus of the ovary and sends small canals arranged like the teeth of a comb toward a larger duct which

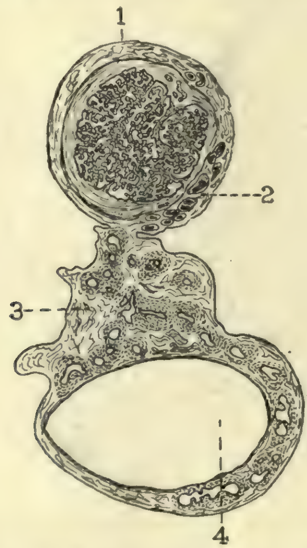


FIG. 57.—TRANSVERSE SECTION THROUGH FALLOPIAN TUBE AND MESOSALPINX SHOWING EPOÖPHORON AND SMALL "PAROVARIAN" CYST. (L.P.) 1. Transverse section of ampullary part of tube. 2. Vessels in wall of tube. 3. Mesosalpinx containing many tubules of epoöphoron. 4. Beginning parovarian cyst (dilated tubule of epoöphoron).

runs parallel to the fallopian tube (wolffian duct, see Fig. 15, p. 27, and Figs. 60 and 61, p. 70). Its cephalad end may form the hydatid of Morgagni. Breaks in continuity are frequent (Fig. 57).

The canals are narrow, thick-walled, and lined with a cubical or low cylindrical epithelium; occasionally the margin is ciliated. The wall is of connective tissue, thick and in the adult may contain muscle fibers. The lumen may be dilated and be encroached upon by low papillae (Fig. 58).

The Paroöphoron is composed of a few small, scattered remains of canals and glomeruli situated in the broad ligament close to the pelvic wall, along the course of the ovarian vessels (Fig. 61, p. 71).

Gaertner's Duct (wolffian duct) runs parallel to the fallopian tube between the layers of the broad ligament, down through the parametrium

and at the level of the internal os enters the substance of the cervix. Usually long breaks in continuity occur throughout its course. In the supravaginal

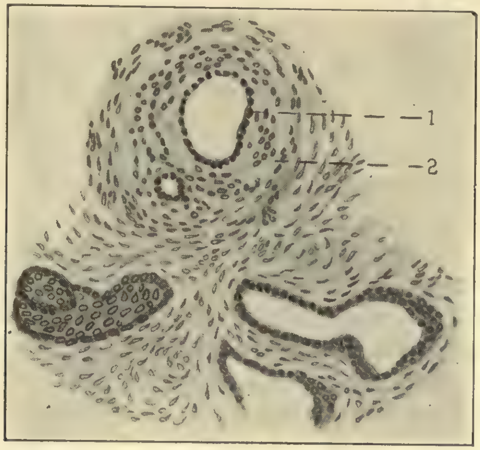


FIG. 58.—TUBULES OF EPOÖPHORON. (High power of Fig. 57 (3). Transverse and oblique sections through tubules of epoöphoron (vestigial remains of the caudal group of mesonephric tubules). 1. Epithelium of tubule. 2. Muscular wall.

part of the cervix the canal is close to the mucosa. In the vaginal vault it lies in the lateral vaginal wall, gradually, as it descends, coming to lie more posteriorly and finally ends by making a sharp curve forward into the side

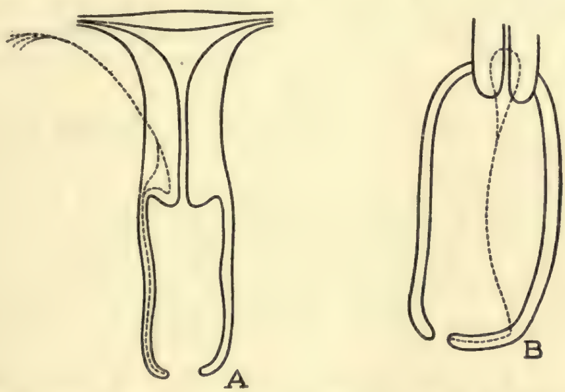


FIG. 59.—COURSE OF GAERTNER'S DUCT: Diagrammatic. From R. Meyer, Arch. f. mikr. Anatomie u. Entwicklungsg., 1909, LXXIII, 751. A. Frontal section showing duct (dotted) from its origin at the epoöphoron running through broad ligament, parametrium, uterine and cervical wall (ampullary dilatation), alongside the vagina and ending in the hymen. B. Sagittal section of lower course of the duct and its relation to the lateral vaginal wall.

of the hymen (Fig. 59, A and B). In the lower part of the cervix the duct is dilated, slitlike (Ampulla, Fig. 23, (3), p. 36).

The epithelium is cubic with dark protoplasm, the nucleus rich in

chromatin (Fig. 24, p. 36). In the vaginal part great variation in the epithelium is found (multilayered, cubic, cylindrical, or squamous).

The musculature is well developed.

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CHAPTER IV

THE RELATION OF THE NORMAL HISTOLOGY OF THE FEMALE GENERATIVE TRACT TO SYMPTOMS AND PHYSIOLOGICAL FUNCTION

The preceding chapter dealt with the anatomy of the female genitalia during childhood, puberty and old age. In order to comprehend the pathological changes which these organs undergo, it is essential to know, and to bear in mind constantly the further variations which occur in response to purely physiological requirements. These functional changes are so striking that they readily impress the uninitiated as pathological. When further complicated by morbid processes, engrafted upon them, a correct interpretation is sometimes impossible.

The best method by which to approach this difficult subject intelligibly will be first to outline the clinical phenomena, next to present the gross and minute changes which accompany them, and lastly wherever possible, to refer to the underlying physiological causes, which bring about both the symptoms and structural variations.

Only in recent years have sufficient facts accumulated to permit of such generalization, nor may we forget that large gaps still exist in our knowledge, which we can bridge only by conjecture. Some points still rest upon a very weak foundation, but taken in conjunction with the whole, they yet serve as a useful skeleton to aid in the support of the entire framework.

In the female generative system, we repeat, the study of anatomy, both gross and microscopic, and of physiology are so intimately blended, that separation is impossible, and a joint consideration of the two becomes necessary. It is, therefore, essential to treat these subjects together, and wherever possible to set forth clearly how unmistakably and rapidly functional requirements react upon anatomical structure, and how the two together produce clinical symptoms which we have accepted as a matter of course.

Classification.—The periods to be considered may be grouped in the following way:

1. EMBRYONIC	Undifferentiated	3rd to 16th week.
	Differentiated	1st to 3rd week.
	Prenatal	16th week on.
2. INFANTILE	Postpartum	Short period of activity.
	Infantile	Passive growth.
	Prepuberty	Preparatory to generative function.

3. PUBERTY	Cyclical (menstrual)	Premenstrual.
		Menstrual
		Interval.
	Gravidity	Nidation.
		Diffuse chorionic.
		Placental.
	Post-partum	Early involutionary, puerperium
		Lactating.
4. SENILE	Regressive	

I. EMBRYONIC.—1. *Undifferentiated.*—The internal generative organs are formed (in conjunction with the urinary system) from parts of the wolffian and Müller's ducts (Figs. 60 and 61). During the first few weeks of

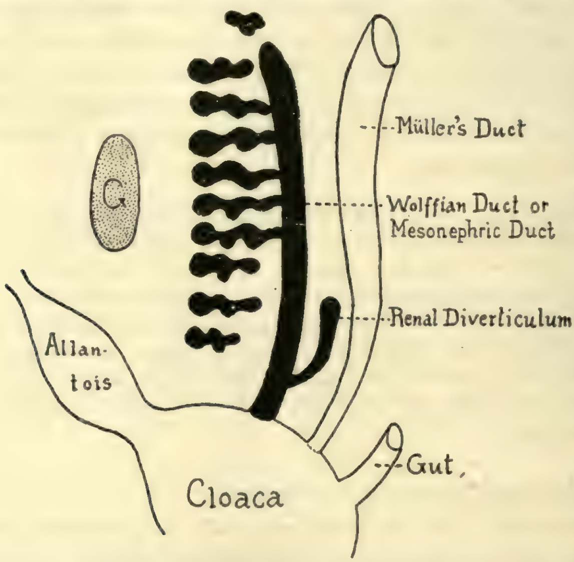

FIG. 60.—DEVELOPMENT OF THE SEX ORGANS. INDIFFERENT TYPE. Diagrammatic. *G*=sex gland. Figs. 60 and 61 (modified from Wiedersheim).

embryonic life no difference between the male and female sex can be noted (Fig. 60). By the third week, however, the ovary and testis can be distinguished by their microscopic structure. The external genitals show recognizable differences by the end of the fourth month.

2. *Differentiated.*—The ovarian anlage arises from special cells of the peritoneal cavity. These cells proliferate and in the lower forms which lend themselves to study, it has been claimed by some that special cells which ultimately form the reproductive cells wander through the mesoderm until they reach the ovary (Fuss, 1). In the chick, Swift (2) claims that these sex cells originate in the extraovular portion of the membranes.

The fallopian tubes, uterus, and vagina are formed from Müller's duct (Figs. 60, 61, 62, and 63). Fusion of the two ducts in the second month

of fetal life produces the uterus and vagina (Fig. 65). The vulva arises independently from the external skin structure. The hydatid of Morgagni, the epoöphoron and paroöphoron are the vestigial remains of the wolffian system (Fig. 61). See also Chap. III.

3. *Prenatal.*—The generative organs during the last two months of intrauterine existence, closely resemble those of infants up to the second year. Graafian follicles in small numbers are found in the ovary (Deléstre (3)). In the ninth month the gonad descends to just above the pelvic brim. The tubes, uterus, vagina are similar to those of the infant though slightly smaller in size.

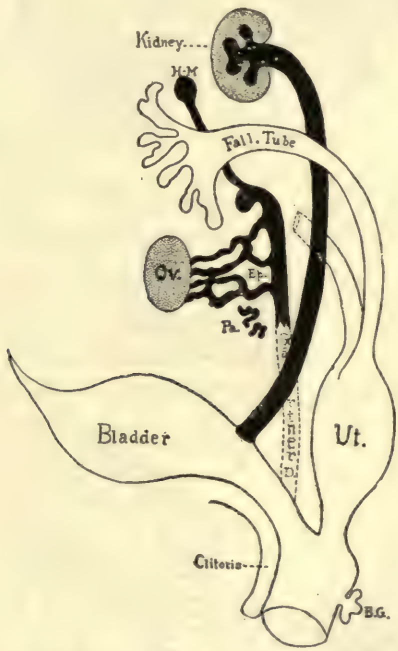

FIG. 61.—DEVELOPMENT OF THE SEX ORGANS. (Female Type.) Wolffian derivatives in solid black. Müllerian derivatives in outline. H.M., hydatid of Morgagni. Ut., Uterus. B.G., Bartholinian gland. Ov., Ovary. Ep., Epoöphoron. Pa., Paroöphoron.

4. *Physiology.*—The physiological significance of the fetal generative organs in utero has not been studied. Experimentally no method has yet been devised to permit of such research. Possibly the technic of Carlson who removed the pancreas of the mother and found the post operative sugar delayed and diminished might be utilized (4). He ascribes this delay to the activity of the fetal pancreas. Similar experiments by Werelius appear to show that the fetal parathyroids are inactive. Nature occasionally enables us to make limited observations—hermaphrodites, hybrids, absence of genital glands—but as yet no attention has been given these rare occurrances, and coincident with the genital defects so many other abnormalities exist, that no safe physiological deductions can be drawn. Very possibly

the action of the ovaries of the mother, transmitted through the placenta, by means of an internal secretion, far outweighs any effect which might be exerted by the presence or absence of the small and inactive fetal gonads.

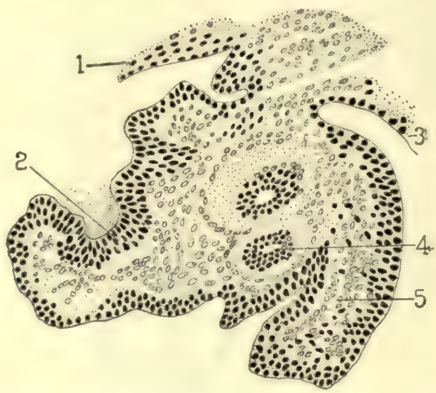

FIG. 62.—TRANSVERSE SECTION THROUGH ANLAGE OF RIGHT MÜLLERIAN DUCT, 10 mm. HUMAN EMBRYO. 1. Lateral body wall. 2. Müllerian groove. 3. Mesentery. 4. Mesonephric tubule. 5. Genital gland. (Redrawn from Prentiss and Arey.)

Nevertheless it must be borne in mind that children of mothers in whom the ovaries were removed early in pregnancy show no abnormalities.

II. INFANTILE.—1. *Postpartum.*—Immediately after birth the genitals of a female fetus (5) evince a short period of activity which may continue

FIG. 63.—SAME AS FIG. 62 BUT THREE SECTIONS CAUDAD SHOWING TUBULAR ANLAGE OF DUCT. 1. Müller's duct. (Redrawn from Prentiss and Arey.)

for one or several weeks. The cervix secretes a varying amount of mucus; the endometrium becomes hyperemic, not infrequently to such a degree that bloody vaginal discharge results. The breasts may become engorged and

painful, and then secrete colostrum-like fluid. The ovaries, however, evince no special changes.

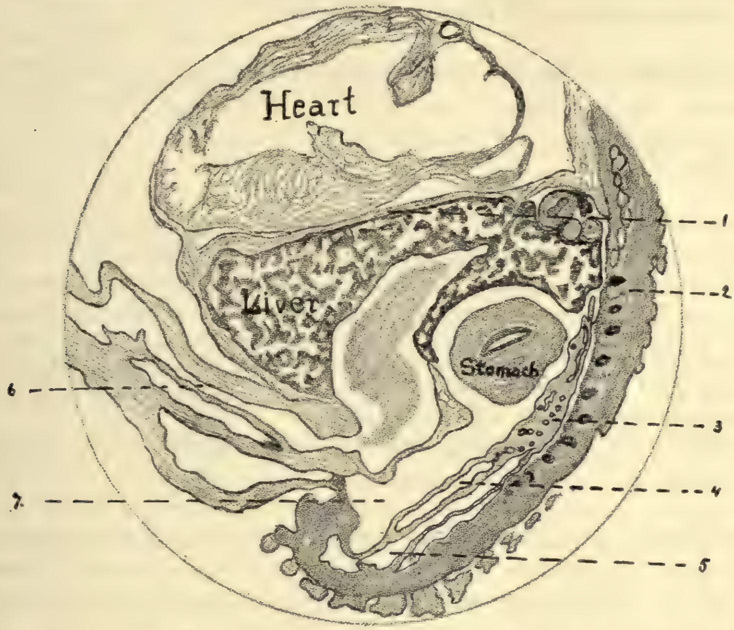

FIG. 64.—EXTRAMEDIAN SAGITTAL SECTION OF 9 mm. (HEAD RUMP) HUMAN FETUS. (L.P.) Shows relation of mesonephros (wolffian body and duct) to other organs. 1. Diaphragm. 2. Vertebral column. 3. Mesonephros and its tubules. 4. Mesonephric duct. 5. Vein. 6. Umbilical cord and vessels entering liver. 7. Abdominal cavity.

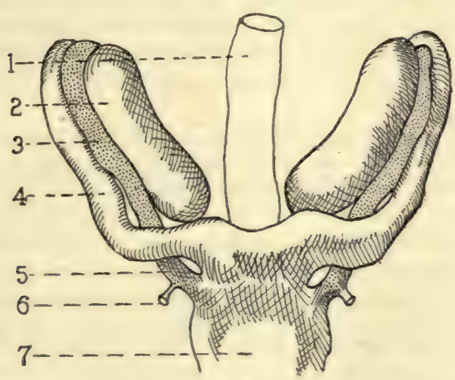

FIG. 65.—SEX ORGANS OF FEMALE EMBRYO, SECOND HALF OF THIRD MONTH. Müller's ducts have already fused to form the uterus and vagina. The wolffian ducts persist showing their relation to the ovary, tube and uterus. 1. Intestine. 2. Ovary. 3. Wolffian duct. 4. Müller's duct (fallopian tube). 5. Course of wolffian duct below tube. 6. Round ligament. 7. Uterus. (Redrawn from Poirier and Charpy.)

Physiology.—These phenomena are quite normal and, until recently, have been ascribed to the change from the intrauterine, placental, to the postnatal independent circulation with consequent readjustment of blood supply (due to obliteration of the

hypogastric vessels, etc.). At present two views are entertained. Halban (6) believes that, after birth, the inhibitory influence of the internal secretion of the placenta is removed, with the above result. Others consider that the withdrawal of the mother's ovarian secretion produces this transitory activity (7).

2. *Infantile.*—After the disappearance of the postpartum excitation of the genitals, there follows a long period of slow passive growth, which on the whole, lags behind the growth of the remainder of the body during these years.

The ovary slowly increases in size, and, except for the fact that no ruptured follicles or corpora lutea are found, the organ resembles a miniature adult ovary.

The uterus, likewise, gradually enlarges, retaining the characteristics of the so-called "infantile type." (See Fig. 20, p. 32.) Compared to the uterine body the cervix is large (3 to 1), the cervical angle is barely indicated, the infravaginal part of the cervix is disproportionately long. The corpus uteri is flat, its mucosa thin, the glands few in number and almost straight tubular in their course. The uterus is still an abdominal organ resting in the false pelvix (see Chapter III).

The tubes and *vagina* are smaller, but otherwise do not differ greatly from the adult type.

Physiology.—The growth of the sex organs during infancy is directly controlled by the internal secretion of the ovaries. This is abundantly proved by castration of animals, and by the rare cases in which castration has had to be performed on very young children.

Under these conditions the genital tract not only fails to develop further, but extreme atrophy supervenes, to such a degree that the uterus, tubes and vagina can barely be distinguished, and the external genitalia remain small, friable and atrophic. In this connection the influence of the follicle epithelium (growing graafian follicles) and possibly that of the interstitial cells (theca and stroma lutein cells) must be taken into consideration.

On the other hand pathological variations demonstrate that *the ovaries are not the sole controlling factors,* for in tumors of the epiphysis cerebri and in adrenal tumors premature sexual ripening (recognized by the appearance of all the changes accompanying puberty has been observed as early as the second year (Lenz, 8). Early puberty independent of demonstrable lesions in any organ, also occurs, though very rarely (l. c. 8). The relations of the various glands of internal secretion to the ovaries will be fully discussed in succeeding pages, but it must never be forgotten that, whatever other stimuli may produce abnormal activity of the genital organs, they require the presence of the ovaries (exceptions to this are offered by experimentally obtained results due to injection of ovarian or placental extracts in castrates).

3. *Prepuberty.*—This stage usually of short and variable duration, may entirely escape clinical observation. Theoretically it would correspond to the time elapsing between the complete maturation and the first rupture of graafian follicles; practically it begins with the time at which "budding into womanhood" is first noticed and ends with the onset of the first menstruation.

During this period the uterus changes from the infantile to the adult type, the breasts enlarge, the distribution of the subcutaneous fat becomes characteristic, growth of hair on the mons and axillae takes place, etc. In other words, the secondary sexual characteristics develop. The psyche, likewise, alters, so that at least subconsciously the sex instinct and inclination fully develop.

Apparently these changes are all brought about by the suddenly increased activity of the ovary, but the primary stimulus is unknown.

III. PUBERTY.—*Puberty* is the period at which the generative organs are ready to fulfill the function of reproduction. The name is commonly applied to the period marked by the occurrence of the first *menstruation.* In some instances, however, in which the menstruation is delayed or remains in abeyance, although ovulation occurs, the prepuberty and the puberty stage cannot be differentiated clinically. The *period of sexual activity* extends from the onset of puberty to the development of senile involution (corresponding loosely to the onset of the *menopause*).

Menstrual Cycle.—In all animals except in anthropoid apes and the human race, the sexual and reproductive function is periodic and limited to certain seasons of the year (9). The remains of the cyclical arrangements show themselves in the human female only in the occurrence of menstruation, although in certain highly primitive races which exist under conditions of rigorous environment (Eskimo, Australian aborigines) slight remains of the original sexual season can be recognized (conception usually occurring during spring, harvest feasts accompanied by sexual rites, no menses in winter, etc. (l. c. 9)).

Onset of Menses.—The period at which menstruation begins varies according to race, climate and immediate environment. It usually falls between the ninth and fifteenth year; is early among southern races (East India, Central Africa, Jews, etc.), later in northern climates (10). Among people of similar race the menses appear earlier in city than in country dwellers. Great individual variations are the rule.

The clinical symptoms which occur during the menstrual cycle are well known. The histological changes, which account for the visible manifestations (such as increased secretions, bleeding, etc.) have lately been the subject of close study and are now better understood, but the physiological basis of the entire process is still a subject of dispute. With the aid of recent investigations on animals, a fairly comprehensive and well-founded conception can, however, be obtained, and correlation of symptoms, structure and function can be shown.

Duration of the Menstrual Cycle.—In a given individual during health, the time elapsing between successive periods is the same. Twenty-eight days is the most frequent variety, but 21 and 30 to 35 days are not unusual.

Clinical Signs of the Menstrual Cycle.—A few days or hours before the onset of the menses a feeling of pelvic heaviness is felt by the woman. This is the premenstrual period. Increased vaginal (i.e., cervical) discharge is commonly noted. In some individuals the breasts enlarge and become sensitive. The thyroid gland may swell during

each cycle. Psychical disturbances, such as slight irritability, increased sexual desire and mental hyperactivity or lassitude are physiological. Transitory pigmentation is not uncommon.

Menstrual.—The onset of menstruation closely corresponds to the appearance of blood in the vaginal discharge and is known as the *menstrual period.* The blood is normally dark, mixed with cervical secretion and not coagulable (11). The bleeding persists for hours or days (1 to 8 days), usually for the same period in a given individual. In certain cases a distinct relief, comparable to the deturgescence following orgasm, is felt after the flow is established.

The amount of blood passed, according to Hoppe-Seyler averages 37 c.c. during a menstrual period. Traces of arsenic have been reported in the menstrual blood (12).

After the bleeding has ceased the quiescent or intermenstrual stage begins, and lasts until the next premenstrual time. It is sometimes called the interval. There are no subjective phenomena in the healthy woman, during this time. Many authors consider the period immediately following menstruation as the most favorable for conception (13).

FIG. 66.—TRANSVERSE SECTION, ADULT UTERUS: RESTING STAGE. (×10.) Note roomy uterine cavity, thin mucosa with glands straight and far apart. Peripherally is musculature.

The uterus during the premenstrual period becomes perceptibly larger in size, an increase in some instances reaching one-third above the normal resting dimensions. The cervix feels softer to the touch, and the external os is patulous and even Hegar's sign may be simulated. The entire pelvis, as far as it is accessible to the examining finger, gives the impression of hypervascularity and pulsation. Frequently one of the ovaries appears enlarged and tender (ripe follicle?).

When the menstrual flow begins, the uterus rapidly grows smaller and harder. It remains hard and small throughout the intermenstrual period.

HISTOLOGICAL CHANGES OCCURRING IN THE UTERUS DURING THE MENSTRUAL CYCLE.—Greatly divergent views are at present held on the subject. Our endeavor will be to present the essential facts in the simplest way, and in a fashion best calculated to accord with clinical requirements.

Histologically, the uterine cycle may be divided into three periods—the intermenstrual, the premenstrual and the menstrual (l. c. 13).

The Intermenstrual Period begins immediately menstruation ceases, and ends with the premenstrual changes, which manifest themselves 4 to 6 days before the onset of the flow. The picture presented by the mucosa corresponds to that given in the older textbooks as the normal type. The mucosa is thin (Fig. 66), the glands are far apart (the interval between individual glands corresponding to about 4 or 5 times the diameter of a gland on transverse section), their course is straight. The gland cells form a single layer of columnar epithelium, with centrally located, deeply staining nucleus. The gland lumen is empty (Fig. 68).

The interglandular connective tissue is composed of closely packed lymphoid cells, the nucleus of which is prominent, the cell body not being visible.

FIG. 67.—SAME AS PRECEEDING FIGURE: SECRETORY STAGE. Note tortuous and slitlike uterine cavity almost obliterated by thickening of mucosa. Thickening is due to increased vascularity, succulence of cells and hyperplasia of glands.

The Premenstrual Period or Period of Secretory Activity does not set in abruptly or equally in all parts of the endometrium. Individual glands increase in size and tortuosity, consequently, by the time that this change becomes generalized, the glands are in close approximation and give a varied and bewildering picture. Not only are the gland outlines irregular and sinuous, at first corkscrew, later convoluted with contracted and dilated segments, but their epithelial lining shows equally startling changes (Fig. 69). The epithelial cells increase in size, their boundaries toward the gland lumen are irregular and less distinct, the nucleus stains poorly and the cell body is distended with secretion. Toward the end of the premenstrual period the epithelial activity is so great that groups of cells are forced outward toward the lumen forming projecting clusters termed pseudo-papillae. The gland lumen is filled with secretion, consisting of mucus, partly disintegrated cells and detritus. In both the surface and gland epithelium mitoses are common. They can be distinguished only in thin and well-stained sections.

The stroma simultaneously undergoes equally striking changes. The cell body of the lymphoid cells increase in size, therefore the nuclei are less closely packed, cell boundaries are visible, and individual cells can be recognized. The changes first occur and always remain most marked beneath the surface epithelium and around the circumference of the

capillary vessels. They are never equally developed in all districts. The changed cells are termed *decidual cells* and were formerly considered pathognomonic of pregnancy (Fig. 70).

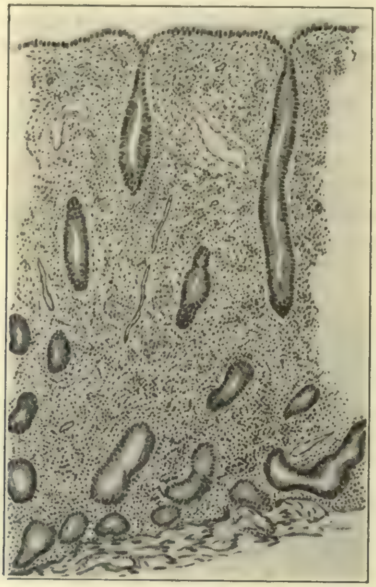

FIG. 68.—SECTION OF NORMAL RESTING MUCOSA OF UTERUS. (M.P.) Note surface epithelium, narrow mouth of glands, the big interglandular distance, change of direction of gland fundi, connective tissue stroma, muscle.

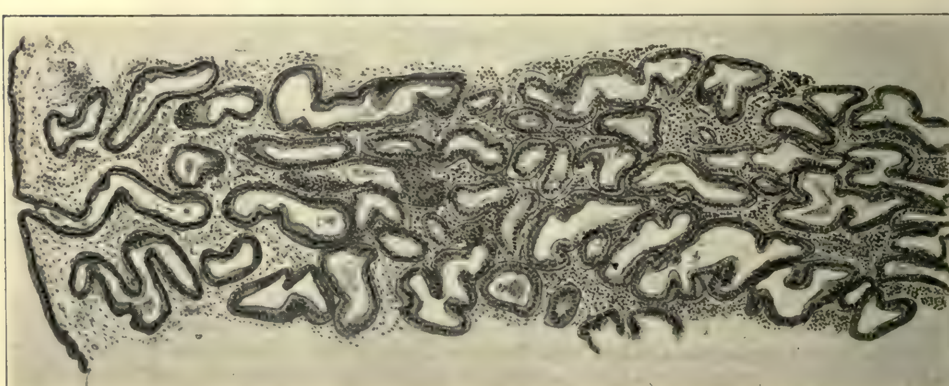

FIG. 69.—SECTION OF NORMAL MUCOSA, SECRETORY STAGE. (M.P.) Note increase in thickness of mucosa (compare with Fig. 68), in number, size and tortuosity of glands, small interglandular distance, edema near surface, small amount of secretion in gland lumina.

Toward the end of the premenstrual period the capillaries of the endometrium become plainly visible, because they are clogged by innumerable red blood cells. As the stasis (and probably, the permeability of the vessel wall) increases, edema of the stroma develops, so that at the onset of the menses the picture presented is that of secretory hyperactivity,

engorgement and edema. Specimens obtained from mucosae during this cyclical phase were formerly classified as "hypertrophic or hyperplastic endometritis."

Menstrual Period.—Red blood cells are found in all the tissue spaces, singly and in large groups, sufficient to obscure most other details. The red cells are particularly

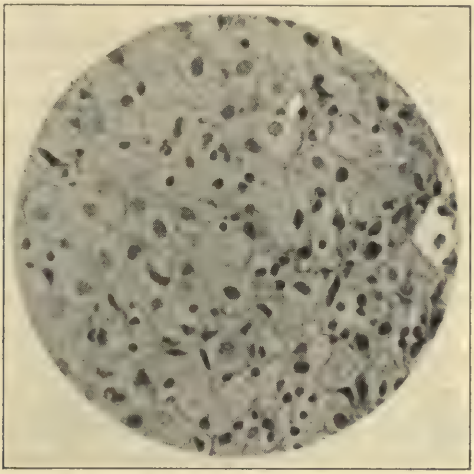

FIG. 70.—DECIDUA: UTERINE STROMA IN LATE PREMENSTRUUM OR EARLY PREGNANCY. (H.P.) The stroma cells show a large cell body, clear cut cell outline and light staining nucleus.

numerous beneath the surface epithelium, and then appear within the lumen of the uterus (Fig. 71). No large losses of substance occur and subepithelial hematomata, such as were described by Gebhard are not frequent in carefully obtained or well preserved specimens. Red cells are numerous in the gland lumina. Schroeder (14) claims that all

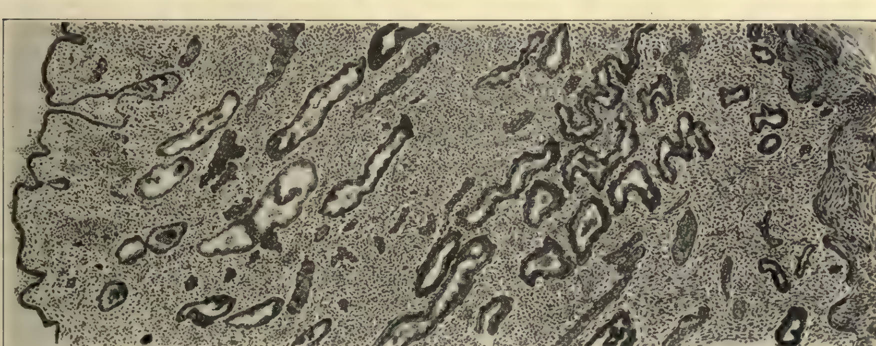

FIG. 71.—SECTION OF NORMAL MUCOSA AT ONSET OF MENSTRUATION. (M.P.) Note beginning appearance of r.b.c. in uterine cavity at upper edge, engorgement of vessels of mucosa, diffuse distribution of r.b.c. throughout the stroma. Uterine glands still show corkscrew-like outline and pseudopapillation characteristic of premenstruum. Glands and stroma close to uterine muscle remain unchanged.

but the basal layer of endometrium is destroyed at each menstruation. Robert Meyer (Arch. f. Gynäk., 1920, 113, 259) accepts Schroeder's findings and agrees that the functional part of the uterine mucosa is cast off at each menstruation. The *premenstrual*

change is termed *pregravid* by Meyer, in order to emphasize the purpose of the change, which occurs to offer a favorable bed to an impregnated ovum.

The glands, at the onset of the menstrual flow, rapidly empty themselves of their secretion and the gland epithelium, within a few hours, or at most within one or two days, returns to its simple columnar type. At the same time the stroma loses its succulence, and again resumes the inactive lymphoid form.

Variations.—As none of the three periods begin abruptly, or are equally developed throughout every portion of the interior of the uterus, it will be readily understood, that uniform pictures are the exception and not the rule. The phase must be recognized from the type prevailing in one, or preferably more sections taken from different parts of the uterus.

Physiology.—No chapter in physiology is more interesting, or is less understood than the one dealing with the menstrual cycle. Without recourse to comparative studies and experiments on animals, it would still remain a closed book to us. At the risk of appearing prejudiced, we prefer to present our views, rather than to enter into a long and necessarily involved exposition of all the theories and hypotheses still current. Only such facts as are best established, will be mentioned and woven into a theory, which, though not universally accepted, has the support of numerous physiologists. Many of these observations have been made on lower animals, and have not, as yet, been substantiated in the human being. Probably numerous revisions in our views will be necessitated by increase in our knowledge. Let us first give the theory, and then substantiate it by the facts upon which it is based.

Theory.—The menstrual cycle is dependent primarily on the activity of the ovaries. Even in infancy and before the onset of puberty the ovaries exert a growth-stimulating or protective influence on the rest of the genital tract.

The onset of *puberty* is inaugurated by an internal secretion arising from the full maturation of repeated crops of graafian follicles. Perhaps also the ovarian influence is assisted by the action of one or more of the other ductless glands (l. c. 13).

After these repeated stimuli have prepared the soil for the generative function, the onset of menstruation is finally ushered in *by maturation of one or more follicles which cause the premenstrual uterine changes.*

Rupture of the follicle coincides with or closely follows after the menstrual flow.

During the formation and the active (chemical) secretory stage of the corpus luteum (a period of from 10 to 14 days) *the uterine mucosa is ready and able to receive and embed the ovum.* During the active stage of the corpus luteum, follicles are inhibited from ripening, and menstruation is, therefore, postponed until the yellow body begins to regress. If no fertilized ovum is at hand, or if the ovum fails to embed, new follicles mature and the cycle is repeated. If, on the other hand, a fertilized ovum becomes embedded, *the corpus luteum persists* and hence the menstrual changes merge into the changes which accompany pregnancy.

A summary of these postulates would read:

1. Full maturation of follicles causes the premenstrual changes.
2. Follicular rupture coincides with, or follows closely the onset of the menstrual flow.

3. During the active growth of the corpus luteum.
   (a) The uterine mucosa is sensitized, so as to be capable of receiving a fertilized ovum.
   (b) Follicle ripening is interfered with.
4. During pregnancy the corpus luteum persists, follicular ripening is, therefore, interfered with, and hence the menstrual cycle is postponed.

The proofs to be adduced to this theory are:

Full maturation of follicles causes the premenstrual changes.

We know from castration, as practiced on human beings and animals, that both the development of the genital organs and the menstrual or estrous cycle (15) *is dependent on the ovaries—on the entire gland.* By exposure of the ovaries to the X-ray *we are able to destroy the maturing follicles,* in which case menstruation or estrus is delayed until a new crop of follicles matures. Further exposure to the rays—sufficient to destroy even the very young and unripe follicles, produces protracted or permanent cessation of menses or estrus (artificial menopause), *although atrophy of the genitals then rarely reaches the degree attained after castration.*

From these and other experiments (16) we are justified in concluding that *maturation of follicles prepares the uterus for the menstrual act;* and that some other constituent of the ovary (perhaps the *interstitial gland,* in certain species, 17), has a trophic influence on the genital tract.

Follicular rupture coincides with or closely follows the onset of the menstrual flow. No direct proof of this postulate can be given. We are forced largely to resort to circumstantial evidence obtained from the lower animals. All mammals except man confine their sexual congresses to definite periods (estrus or rut). Estrus, or rather the pro-estrum which corresponds to menstruation proper, gives sufficient external signs to be readily recognized. In some animals—bitch, cow, monkey—a bloody flow occurs, thus further emphasizing the relationship.

In all the forms so far studied, estrus and follicular rupture coincide. In some species—especially rodents—coitus materially assists rupture of the follicle.

Hence, unless during evolution, the human race has lost this relation between follicle rupture and menstruation, (and many authors believe that the fact that the human species no longer confines its sex-relation to a definite cyclical period goes to prove this) the general law should apply. The researches of Robert Meyer (18) and of others (19) on human material has lent additional evidence to this view. In a large series of cases recently ruptured follicles or very early corpora lutea were regularly found from one to ten days after menstruation.

During the active growth of the corpus luteum the uterine mucosa is sensitized so as to receive the fertilized ovum. The experiments of Fränkel (20) first drew attention to the fact that nidation (embedding of the ovum in the uterine wall) depended to a great extent on the presence of the corpus luteum. His experiments and deductions were, however, faulty.

The work of Leo Loeb (21) has conclusively demonstrated the course and significance of the phenomena.

From about the tenth to the fourteenth day after follicle rupture (variation as to time will probably be found in different species—the guinea pig, rabbit and rat (l. c. 16) so far having alone been investigated)—the uterine mucous membrane *reacts to trauma* (foreign bodies, ovum) by producing a decidua which far exceeds in volume the spontaneous estrual or menstrual decidua (experimental deciduomata (21)). If the corpus luteum is destroyed or removed neither the normal or artificial decidual reaction takes place, and therefore, the ovum cannot be embedded.

Follicle ripening is interfered with by several factors, a consideration of which follows. Each species of animal, with slight individual differences, has a definite cyclical period for estrus or menstruation. In rabbits and guinea pigs it is 28 days, in rats 21 days, etc. Loeb has shown (l. c. 13) that by removing the corpus luteum, this period is abridged. He has also shown at least in certain species that, while the corpus luteum flourishes, follicles fail to reach full maturity.

Nature has demonstrated the same fact in a different way. Cows occasionally for months have a persistence of the corpus luteum, without pregnancy. During this time estrus is suppressed. If the ovary is removed, or if the corpus luteum is squeezed out of the ovary, estrus promptly reappears (l. c. 16).

During pregnancy the corpus luteum persists, follicular ripening is, therefore, interfered with, and the menstrual cycle is postponed.

That menstruation is not merely mechanically interfered with by the obstruction presented by the ovum is self understood. If this were the case, intra-uterine accumulations of blood would take place. Again, if this were true, in duplex uteri, with pregnancy in one horn, the empty uterine body would menstruate.

The cessation of menstruation is, therefore, not mechanical. That cessation of estrus, independent of pregnancy, occurs, if the corpus luteum persists, was shown in the preceding paragraph (in cows) and this also demonstrated that the ovum is not the sole factor which can bring about persistence of the yellow body.

Exactly what effect the ovum exerts is not known as yet. Therefore, we are justified, in the present state of our knowledge, in accepting the postulate which heads this paragraph, with the understanding that further research will probably enlarge and modify our views. It is true that some observers have reported rupture of follicle during pregnancy in human beings. These reports are neither numerous nor convincing.

From what has preceded it will be seen that the *ovary does not act as a simple gland.* It combines several functions. Part of the function is purely protective or trophic; part produces the premenstrual and menstrual change; and part controls the further decidual reaction, necessary for the embedding of the ovum, and finally, part exerts an inhibitory effect on cyclical changes, until the end of labor again gives rise to a demand for renewed reproductive activity, thus preventing waste of follicles, or possible interference with pregnancy due to the engorgement produced by ripening follicles.

In the present connection, that function of the ovary which has to do with the elaboration and maturation of the ovum *per se* has not been dealt with.

IV. **Gravidity.**—*General Considerations.*—Two essential factors are needed for successful gravidity, first a fertilized ovum, and, secondly, a sensitized mucous membrane. Normally this is the uterine mucosa, though under pathological conditions, in the human race, the mucosa of the fallopian tube, the follicles or the stroma of the ovary or even the peritoneum may be selected as the implantation site, if they become sensitized (see p. 445).

For a description of the process of fertilization and the changes occurring in the ovum, the reader is referred to textbooks of Embryology.

When the fertilized ovum reaches the uterus at a time at which the mucosa is sensitized, its first action may be regarded as purely mechanical.

This foreign body action calls forth the decidual responses, necessary to form the maternal part of the placenta (Loeb) at least in deciduates (21).

Before considering the mode of action by means of which the ovum attaches itself within the decidua, it is expedient to consider the various general and local changes which accompany the process.

The Changes Which Take Place During Pregnancy:

A. *General Systemic*
- *a.* Heart and other organs.
- *b.* Breast.
- *c.* Glands of internal secretion.
- *d.* General secondary sex characters.

B. *Uterine*
- *a.* Mucosa.
- *b.* Muscle.
- *c.* Cervix.
- *d.* Peritoneum.

C. *Local at site of Ovum.*
- *a.* Nidation.
- *b.* Stage of diffuse Chorion.
- *c.* Placental stage.

D. *Associated Pelvic.*
- *a.* Tubes.
- *b.* Ovaries.
- *c.* Vagina and Vulva.
- *d.* Pelvic connective tissue.

A. General Systemic.—Some of the changes produced by pregnancy are quite specific, others are in response to the increased demands made upon the maternal organism by the growing fetus.

The Heart, Vascular System, Liver, Kidneys, etc., show certain changes which appear to be in direct proportion to the additional demands made upon their activity, and which differ in no way from similar changes produced by innumerable causes (22). *The osseous system,* especially the marrow of the flat bones, undergoes changes which are almost specific and pathognomonic of pregnancy, puerperal osteophyte. These may be due to hypophyseal changes.

The Breasts begin to enlarge in the earliest weeks of pregnancy. The increase in size is due chiefly to hyperplasia of the glandular tissue. Observation and experiments have shown that these breast changes are due to the action of the corpus luteum and placenta (l. c. 7). They are seen to a lesser degree in many women during menstruation.

The Glands of Internal Secretion, as far as they have been studied, show distinct functional and at times, organic changes. The intimate relationship and interrelation of the ductless glands has been frequently demonstrated (l. c. 13). The thyroid usually hypertrophies to a moderate degree. Unless this functional change takes place, disturbances occur. The hypophysis likewise increases in size, sometimes to such an extent as to produce

symptoms resembling those of acromegaly. Its chromophobe cells increase enormously in size and number (l. c. 16) and require years to regress.

The adrenals probably undergo regular changes, in most instances purely functional, which, however, have not been sufficiently investigated (l. c. 13). Pigmentation, hypertrichosis, etc., occurring during pregnancy have been ascribed to this hyperplasia. The corpus luteum persists throughout pregnancy. Whether it functionates throughout this period is still an open question. Certainly, removal of one or both ovaries, after the ovum is once firmly embedded (a period which in the human female occupies no more than at most the first two months of gestation), does not interfere with normal pregnancy, labor and lactation (l. c. 13). It would seem that after the process initiated by the yellow body—nidation, breast hyperplasia, have been set in motion, the ovum, or rather the chorionepithelium (as the same occurs in hydatid mole without a fetus) is able to produce the further stimulus unaided.

The Changes in Secondary Sexual Characteristics, accompanying pregnancy, have just been enumerated in connection with the individual glands of internal secretion, which appear to be responsible for their development. Consequently, we must in future consider these changes merely as indices of the degree of stimulation exerted by pregnancy (corpus luteum, chorionepithelium) upon the ductless glands.

B. UTERINE CHANGES.—*The changes taking place in the uterine mucosa are merely a continuation and accentuation of the regular premenstrual alterations.* The mucosa hypertrophies greatly throughout the uterus, but particularly at the placental site (corresponding to the experimental deciduomata previously referred to). Through this hypertrophy the interior of the uterus becomes mammelated and nodular.

The thickening of the mucosa results from the hyperplasia of the three main component parts. The decidual reaction of the stroma is very marked. The glands, in the first months of pregnancy, are enlarged and tortuous, and no small part is played by the enormous increase in size and number of the blood vessels and lymphatics (Figs. 72 and 74).

In early pregnancy even to the naked eye a cross section of the mucous membrane shows two distinct layers, an outer *compact* zone toward the uterine lumen, composed mainly of decidual cells, and an inner *spongy* zone, which is honeycombed by the numerous enlarged uterine glands. (Fig. 74.)

The stroma reaction is more uniform and greater in degree than that occurring before menstruation. The decidual cells are larger, and, therefore, in section, the tissue looks more like an epithelial than a connective tissue structure (Fig. 70, p. 79). In the spongy layer also, the stroma is decidual, excepting close to the uterine muscle, where a narrow strip of tissue retains the original spindle-celled type throughout gestation.

The glands show changes corresponding to those previously described as premenstrual, but to an even greater degree. Neighboring glands are almost in contact throughout the spongy layer (Fig. 72). In the compacta

they are few in number, and some appear to have lost their connection with the uterine lumen. The uterine surface epithelium shows changes similar to that of the glands, and according to most authors loses its ciliary margin early in pregnancy.

The blood vessels are more numerous and greatly dilated, the veins predominating over the arteries. In the neighborhood of the future placental site their walls and endothelium show changes to be described later.

In later pregnancy, as the uterus enlarges and the ovum, surrounded by the decidua reflexa, exerts pressure against the true decidua, the uterine

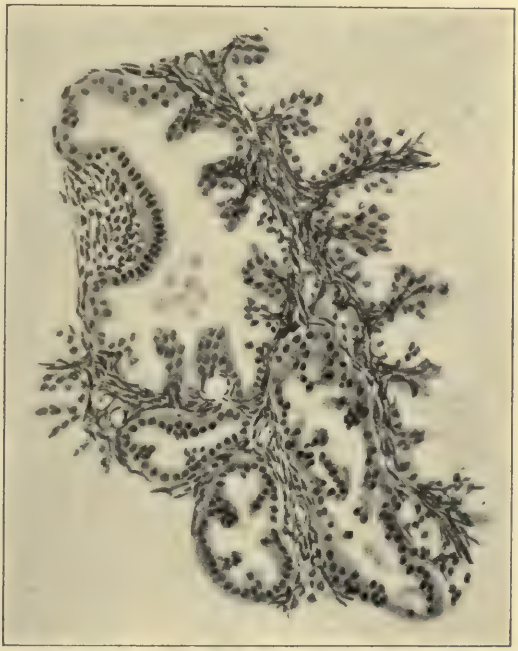

FIG. 72.—SO-CALLED "GEBHARD GLANDS" DUE TO PREGNANCY HYPERPLASIA OF UTERINE MUCOSA. (M.P.) Glands are tortuous, epithelium elevated to form pseudopapillae. In premenstruum similar findings occur.

mucosa, except at the placental site, becomes flattened and thinned out. As will be shown, the decidua capsularis (reflexa), by fusion with the vera, obliterates the surface epithelium. The compact layer is now thin, the glands flattened, less numerous and running parallel to the muscle. At term the decidua is no more than a few millimeters thick (Fig. 75).

Musculature and Connective Tissue.—The increase in size and thickness of the walls of the uterus are brought about by combined hyperplasia and hypertrophy of individual muscle fibers. The increase in length, by the sixth month may reach 7 to 10 times that found in the virginal uterus. It is possible that new formation of fibers also takes place.

In a few instances *striped* muscle fibers have been noted in the puerperal uterus, near the placental site.

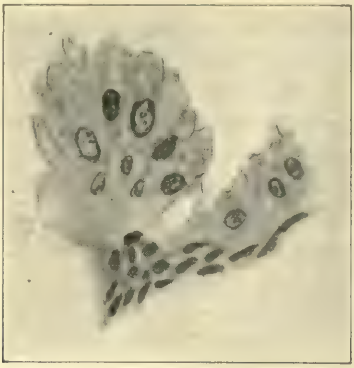

FIG. 73.—HIGH POWER OF GLAND EPITHELIUM OF FIG. 72.

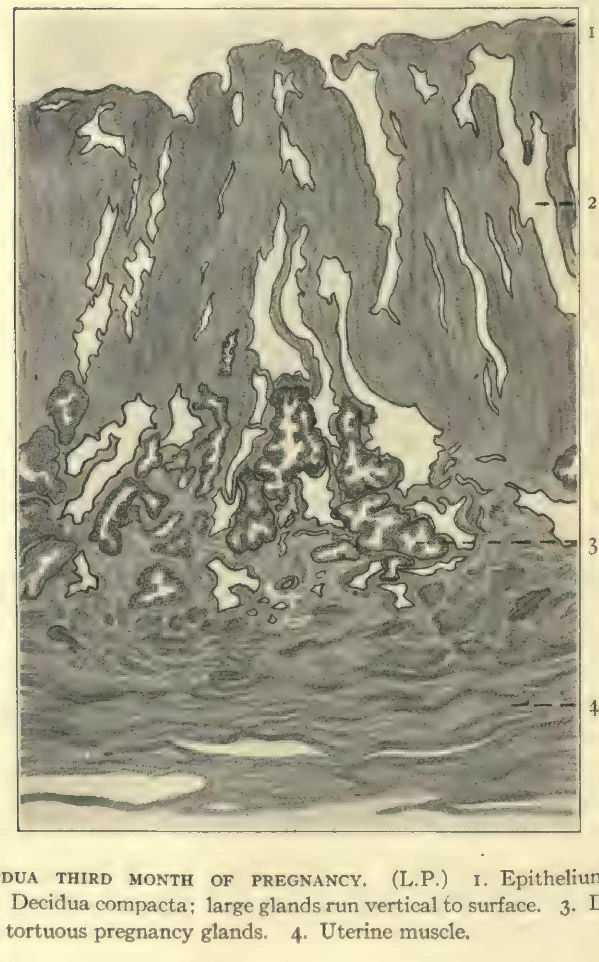

FIG. 74.—DECIDUA THIRD MONTH OF PREGNANCY. (L.P.) 1. Epithelium lining uterina cavity. 2. Decidua compacta; large glands run vertical to surface. 3. Decidua spongiose containing tortuous pregnancy glands. 4. Uterine muscle.

The connective tissue, especially the elastic fibers, increase at the beginning of pregnancy. In the second half of gestation they appear relatively diminished in number.

The Cervix.—The changes enumerated involve the cervix to a less degree than the remainder of the uterus. The cervical mucosa is but little altered, therefore, a distinct decrease in thickness is noted at the junction of the cervical and uterine mucosa. The cervical glands secrete more mucus

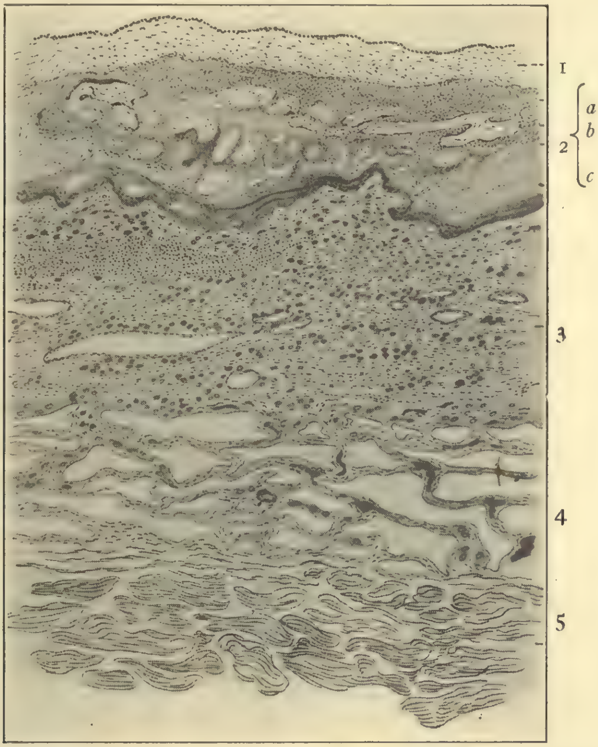

FIG. 75.—FUSION OF DECIDUA VERA AND REFLEXA. (M.P.) The obliterated intervillous space is seen beneath the amnion. 1. Amnion consisting of epithelium toward ovular cavity, and connective tissue toward obliterated intervillous space (2). 2. The obliterated intervillous space contains r.b.c., (*a*). atrophic villi (*b*) and fibrin (Nitabusch's) (*c*). 3. Decidua compacta. 4. Decidua spongiosa. 5. Uterine muscle.

than in the non-pregnant state. The connective tissue is softened, and the muscle fibers are longer. Many of these changes are sufficiently accounted for by the long-continued hyperemia accompanying gestation.

The Peritoneum.—The serous coat of the uterus increases not only in extent (keeping pace with the enlargement of the womb), but also in thickness. Therefore, a hyperplasia of the endothelium and connective tissue must occur. From the fourth month on, tuberclelike gray white nodules are found in the serosa of the uterus, Douglas' cul-de-sac and anterior

rectal wall. They consist of subendothelial groups of decidual cells (see decidua in ectopic pregnancy, p. 449).

C. Local Changes (at Site of Ovum).—The alterations just described must be regarded as the continuation of the premenstrual changes and occur only if a fertilized ovum reaches the uterus. Should no ovum be at hand, and therefore, no continuous stimulus be exerted, menstruation supervenes and the cycle recurs.

The changes brought about by the action of the ovum may be grouped under the heading of *Nidation.* The earliest period of uterine implantation has not been observed in the human being, an ovum at about the end of the second week being the earliest on record.

Comparative studies have, however, enabled us to form a clear conception of even earlier stages.

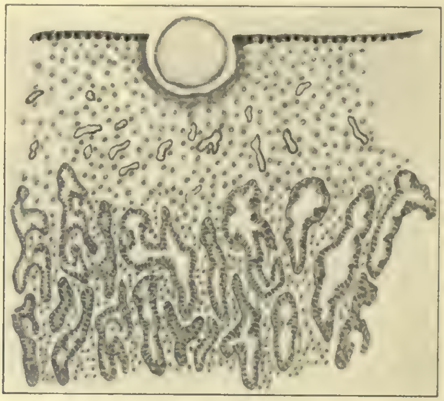

Fig. 76.—Schema of early nidation. Size of ovum greatly exaggerated to show how by lytic action the ovum digests its way into the uterine mucosa (decidua).

Nidation.—The fertilized and segmented ovum reaches a uterus prepared for its reception. Accidental and mechanical factors which vary in each case, determine the exact site of implantation. Usually the ovum becomes attached to the anterior or posterior aspect of the uterine wall near the fundus, but any portion of the endometrium down to and even including the cervix is able to harbor the ovum (placenta previa, cervical nidation) (see p. 457).

The Ovum.—The ovum, perhaps still covered by its zona pellucida, rapidly burrows by means of cytolitic enzyme action into the sensitized mucosa, penetrating beneath the surface epithelium and being arrested in the deeper layers of the compacta (Fig. 76). The point of entry is shut off from the uterine cavity by fibrin, and is soon obliterated. At this period the ovum must still be regarded as a foreign body, and is probably nourished partly by substances it has carried down with itself, from the ovary (23), partly by nutriment obtained by means of osmosis from the surrounding decidua. Very soon, however, the ectodermal layer of the embryo pro-

liferates, surrounding the ovum with a mantle of light cuboidal cells (Langhans' cells) from which arises a spongy, irregular trabeculated tissue—the *fetal syncytium.* This structure shows no cell boundaries, but consists of a continuous layer of protoplasm with multiple nuclei. At a later stage the mesoderm (fetal connective tissue) penetrates the syncytium, probably pushing the Langhans' layer before it, and forms the connective tissue framework of the early villi. The resulting simple projections, the *primitive villi,* soon branch and produce the typical villus. An early villus consists of an outer layer of syncytium. Within this is a single layer of clear, sharply bounded cuboidal cells, *Langhans' cells,* which rest upon the embryonal connective tissue. This connective tissue harbors the fetal blood vessels (Fig. 77).

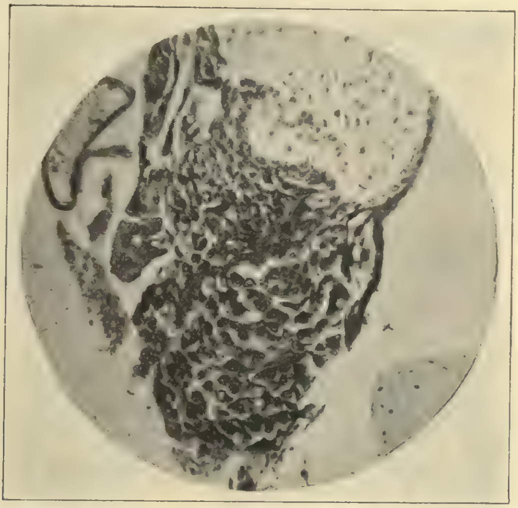

FIG. 77.—CHORION OF 6TH WEEK. Photomicrograph. (H.P.) Above is body of villus with embryonal stroma. A single layer of Langhans' cells covers it. Below is an epithelial mass of intermingled Langhans' cells and syncytium.

The decidua, in immediate contact with the syncytium, shows degenerative changes—coagulation, fibrin formation, loss of cell outlines—and is rapidly displaced by the fetal tissues, probably supplying nutritive material during its absorption. The maternal capillaries are also eroded and, at a very early stage maternal blood is found within channels lined solely by syncytium.

Unfortunately the fetal and maternal cells are morphologically very similar (syncytium and symplasma), digested decidua which has lost its cell boundaries on the one hand, Langhans' cells and decidual stroma cells on the other, so that even when studied in serial section, they appear inextricably intermingled. Hence no exact determination of what should be called fetal in derivation, or maternal in origin, is practicable. This sufficiently accounts for the irreconcilable views entertained by different authors. The relation of ovum and decidua in the earlier stages may be summarized as follows:

1. Period of entrance into the decidua (not observed).

2. Period of loose relation of ovum, covered with beginning syncytium, with the liquefying decidua.

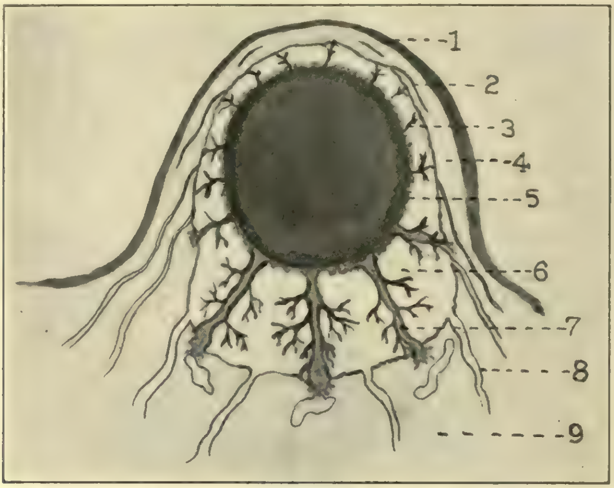

FIG. 78.—DIAGRAM OF PRIMARY INTERVILLOUS SPACE. About the 18th to 21st day. 1. Surface epithelium lining uterine cavity. 2. Obliterated blood vessel in decidua capsularis. 3. Regressing villus. 4. Decidua capsularis. 5. Syncytium covering ovum and lining intervillous space. 6. Intervillous space in future placental region. 7. Anchoring villus in future placental region ("Haftzotte"). 8. Maternal artery emptying into intervillous space. 9. Decidua basalis (serotina).

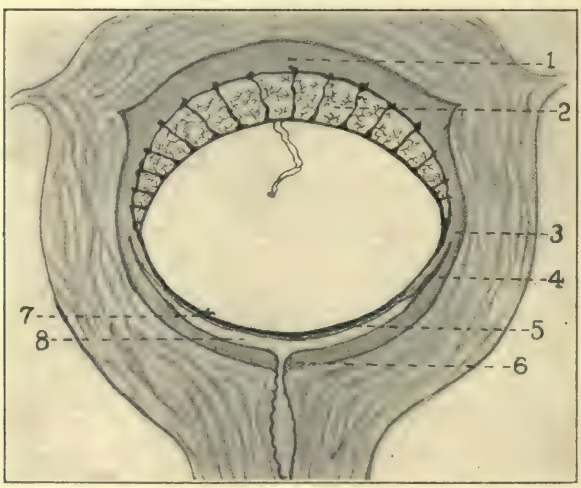

FIG. 79.—SCHEMA OF OVUM IN UTERO AT FOURTH MONTH. 1. Decidua basalis (serotina). 2. Intervillous space of placenta. 3. Fused decidua vera and capsularis. 4. Decidua vera. 5. Decidua capsularis (reflexa). 6. Junction of decidua vera and cervical mucosa. 7. Atrophic chorion and obliterated intervillous space. 8. Remains of uterine cavity.

3. Period of penetration into maternal capillaries during which the spongelike syncytium is imbibing blood, and loose fixation by primitive villi.

4. Period of established maternal circulation, during which the entire ovum is enclosed by the *primary intervillous space.*

Primary Intervillous Space.—The description has already been carried to stage 4. The villi now project into the angiomatous decidua. Possibly they first invaginate the capillary endothelium. At all events this disappears, except where the blood vessels enter or leave the blood chamber which has been formed by coalescence of the many neighboring channels. The ovum may now be likened to a globe, covered with shaggy projections, contained within a larger sphere, to whose walls it is anchored at frequent intervals by large penetrating villi (the "Haftzotten") (Fig. 78). Whether the outer chamber walls are composed of fetal syncytium (Bryce and Teacher,

FIG. 80.—CHORION OF SIXTH WEEK. (H.P.) 1. Syncytial bud. 2. Cross section of villus showing interior stroma and outer layer of Langhans' cells. 3. Langhans' cells of cell islets. 4. Longitudinal section of villus with attached syncytial bud.

etc.) or of maternal endothelium syncytially changed (Pfannenstiel) must remain an open question, although we strongly favor the first view.

Formation of the Discoid Placenta.—The dimensions of the ovum early exceed in size the thickness of the decidua (third to fourth week); consequently this membrane is soon forced outward into the uterine lumen. The decidua capsularis (reflexa) which covers the projecting part of the ovum (Fig. 78) is thinned out; the portion of the intervillous space embraced in this area is consequently narrowed, obstructed and finally obliterated by coagulation (Fig. 75, p. 87). The villi of this region, now cut off from their nutrition, atrophy. By continued growth of the ovum, the capsularis and atrophic chorion is forced against the decidua vera (lining the remainder of the uterine cavity) and by the fourth month fuses with it (Fig. 79). The capsularis, compressed between the vera and the atrophic chorion is reduced to an inconspicuous remnant, so that in the later months the vera and chorion are apparently in apposition (Fig. 75).

Meanwhile, at the pole opposite to the point of entry, the implantation area steadily grows thicker, larger and more defined. The villi multiply in number and in branchings, the capacity of the intervillous space increases proportionately, and the discoid placenta is complete by the end of the third month (Fig. 79). The placenta, as a whole, enlarges until the eighth month, at which time it has reached its maximum.

The structure of the mature villi (Figs. 81 and 83) differs somewhat from that of the earlier ones. The Langhans' cells, except at the point of junction of the penetrating villi ("Haftzotten") with the decidua, disappear. In this location they are noted as broad areas of light polygonal cells (cell islands) (Figs. 80 and 81). The syncytial layer becomes thinned

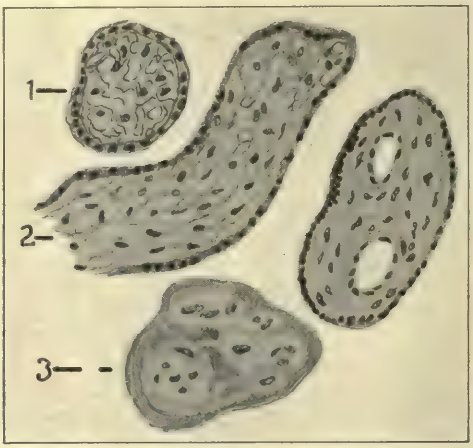

FIG. 81.—VILLI AT FULL TERM: PLACENTA. (H.P.) 1. Cross section of villus; only single layer of Langhans' cells. 2. Longitudinal section of villus. 3. Cell islet embedded in fibrin.

out toward the end of the pregnancy, and disappears in many areas. The stroma is fibrous.

The formation of the body stalk, umbilical cord and amnion does not concern us in this connection.

Toward the end of pregnancy the subplacental decidua (basalis or serotina) undergoes regressive changes. From the earliest beginning of the placenta a fibrinous layer (Nitabusch's "Fibrinstreifen") has interposed between villi and well-preserved decidua. This fibrinous and necrotic area is pierced by the "Haftzotten" and blood vessels (Fig. 82). Toward term, the fibrin increases and the decidua shows necrobiotic changes preparatory to the final separation.

In the third stage of labor the placenta separates in a plane, drawn through the unchanged glands and stroma, which lie in close contact with the uterine musculature. The placental site then consists of an *elevated* raw area composed of only a small fraction of the much thickened mucous membrane. In other parts of the uterus only the surface epithelium is missing.

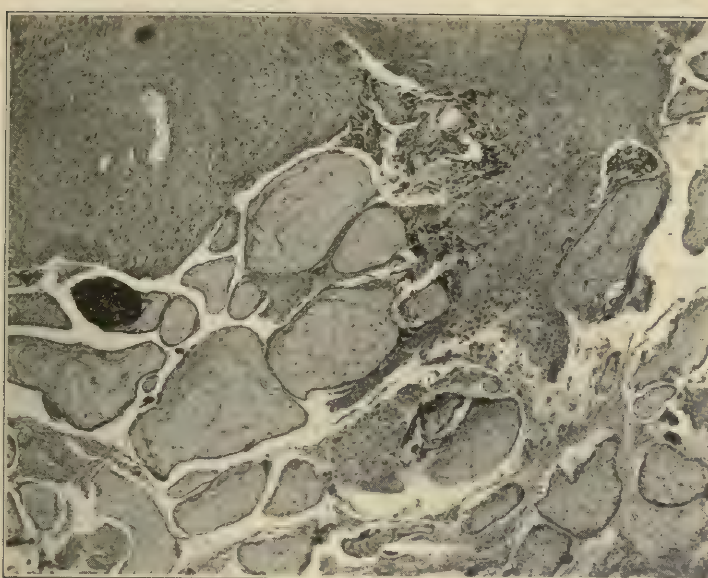

FIG. 82.

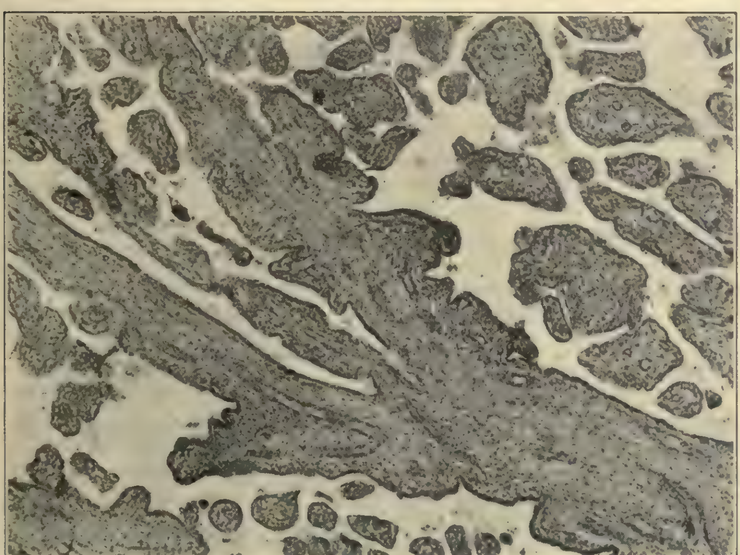

FIG. 83.

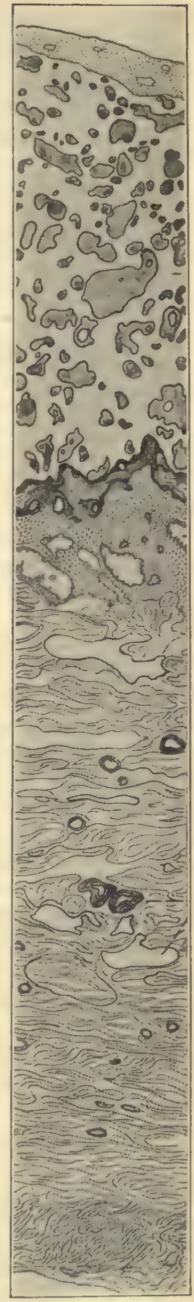

FIG. 84.

FIG. 82—PLACENTA AT FIFTH MONTH. Photomicrograph. (M.P.) Above shows penetration of fetal cells into decidua basalis. (Haftzotte.) Decidua above and to left. Dark areas show calcification.

FIG. 83.—PLACENTA AT TERM. Photomicrograph. (M.P.) Shows adult type of connective tissue composing stroma of villus, low layer of Langhans' cells, absence of syncytium.

FIG. 84.—PLACENTA AT FOURTH MONTH IN SITU. (L.P.) 1. Amnion epithelium. 2. Amnion mesoderm. 3. Intervillous space and villi. 4. Canalized fibrin streak (Nitabusch). 5. Decidua basalis with a few uterine glands. 6. Uteroplacental vessels. 7. Uterine muscle. 8. Peritoneal surface of uterus.

Physiology.—Our knowledge of the physiology of pregnancy is incomplete. So many gaps exist that only a few salient features are as yet clear.

The Decidua.—The sensitization of the connective tissue by the action of the corpus luteum produces a decidua. This membrane apparently has a twofold use. The decidual cells contain a large amount of nutrient substances (especially glycogen) which are absorbed by the ovum in its earliest period of nidation. The decidua, likewise, through its susceptibility to coagulation necrosis, appears to possess the property of resisting the invasive action of the trophoblast.

The Syncytium.—The invasive power of the trophoblast, especially of the syncytium, is quite evident from the morphological picture. Chemical research has also shown that the chorion, up to the fourth month, contains a large amount of trypsinlike ferment, which may enable it to digest the surrounding tissues (l. c. 16).

Physiologically a syncytium has certain special powers. All rapidly growing tissues in which metabolism is particularly active, have a tendency to assume the synctial type. In the new formation of blood vessels, anywhere in the body, syncytial buds are regularly encountered. The syncytial complex is a striking example of the undifferentiated stage of tissue, in which it possesses many of the characteristics of the unicellular organism, a general capacity for metabolic and catabolic activities, which in the higher types of cell are lost or delegated to special organ-complexes. The chorionic syncytium, besides its lytic action appears also to have the power of preventing coagulation of blood, and therefore, can and does serve in place of the vessel endothelium.

The Langhans' cells which must be regarded as the matrix of the syncytium, on the other hand, appear to accelerate coagulation, and probably produce the canalized fibrin streak previously referred to. This fibrinous layer should be regarded as a protective mechanism against too deep penetration.

The syncytium diminishes by the end of the third month, for after the completion of the placenta a tissue with penetrative power is no longer needed or desirable. By the expiration of that time, a very complete and extensive surface for *vascular* exchange has been elaborated. Innumerable, widely branching villi afford an enormous contact surface which is bathed by the maternal blood. The syncytium no longer is called upon to perform the nutritive work of the fetus, which now affects its metabolism by means of its own individual organs, the food supply being obtained from the mother's placental blood (24). The syncytium has consequently regressed, lost many of its primitive functions, and acts merely as a vascular endothelium.

The placenta should be regarded as an organ for exchange—a highly elaborated blood vessel. We personally are inclined to this view, from experimental evidence, which goes to prove that the intracellular ferments of the placenta do not vary to any appreciable degree in response to functional requirements, and that the organs of the fetus contain ferments even in the early months (24). Were the placenta a gland, its ferment contents should increase with increased demand, and decrease under opposite conditions.

A number of investigators regard the placenta not as a mere organ of exchange, but as an elaborate gland, which performs duties for the fetus, comparable to that of the intestine and liver (l. c. 24). The entire matter is still in a state of uncertainty.

The placenta or the trophoblast unquestionably reacts upon the maternal organism. For one thing it causes the persistence of the corpus luteum, so frequently referred to. The means by which this influence is exerted is still shrouded in darkness. Possibly the claims made by Abderhalden may supply the clue. This chemist finds that proteins normally not present in the blood stream, if injected into the circulation even of the same individual from which they were derived, produce a ferment reaction. This reaction though not specific, regularly occurs in pregnancy, and has been ascribed to the continued detachment of minute particles of fetal synctium. This new chemical factor could very well constitute the stimulus we have hitherto vainly searched for. The placenta also contains constituents which produce enormous hypertrophy of all the layers of the uterus (l. c. 7). Apparently corpus luteum and placenta are very similar in some of their actions.

The cause which initiates the onset of labor is also not known. The relation of the ovum to the mother is always unstable. In the early weeks abortion is very frequent, sometimes due to very trifling influences, in other instances often consequent to fetal malformation or death (see p. 463). In the later months, experience has shown that the fetus is able to lead an independent existence even before the seventh month. This tends to prove that whatever forces bring on labor, must act *cumulatively* and are not inaugurated by any sudden change in the fetus. Sauerbruch and Heide have tried to show by artificial symbiosis in animals that the onset of labor is due to an accumulation of substances comparable to those elaborated in fatigue. After the tolerance of the organism has been exceeded, labor pains set in. Their work is by no means conclusive.

From all that has preceded, it must now be evident that the products of conception lead a parasitic existence in the womb of the mother. Like most parasites they produce distinct local and widespread general reactions. The analogy is further strengthened by the fact that disturbances in equilibrium may readily convert this innocent and necessary symbiosis into a process destructive and fatal for its host (chorionepithelioma, p. 471).

3. The Puerperium.—The puerperium begins when the placenta has been expelled, and ends when the genital tract has completely involuted. This period usually lasts from six to eight weeks post partum, but may be protracted for three or four weeks more. At the end of the puerperium the genital system is again ready to resume its reproductive activity.

Gross changes in the involuting uterus.—Immediately after expulsion of the placenta the womb contracts for a few hours. It then relaxes and reaches well above the umbilicus. On succeeding days a rapid and progressive diminution in size occurs (25). The uterus, however, never returns to the size of the nulliparous organ (iii. p. 29).

The main decrease in dimensions results from the involution of the muscle fibers.

Immediately after expulsion of the placenta the vacant site appears as an irregularly circular, raised area about the size of the palm of an adult hand. Its surface shows projections (thrombi protruding from the utero-placental vessels).

The placental site can be recognized for from 2 to 3 months after labor.

The decidua likewise appears as a raw area. Within a few weeks it resumes the aspect of the normal endometrium. By the seventh day it is only 2 mm. thick.

During the first two weeks of the puerperium the raw areas in the interior of the uterus secrete, at first a large, later a constantly diminishing amount of fluid. The discharge does not stop completely until the fourth

week. The lochia, as this post-partum discharge is termed, is first bloody, then serosanguinous, and finally yellowish white.

Numerous abrasions, small tears and interstitial hemorrhages must be regarded as physiological results of labor at term. They occur chiefly at the cervix, vagina and vulva.

Histological Changes in the Involuting Uterus.—Microscopically the immediate reduction in size of the emptied uterus is found to be due to contraction of the muscle fibers. One hour postpartum the individual fibers have contracted to one-half their previous length and are proportionally broadened (l. c. 25). By the end of the third week they are only one-fifth of this length. After the primary contraction, further diminution in

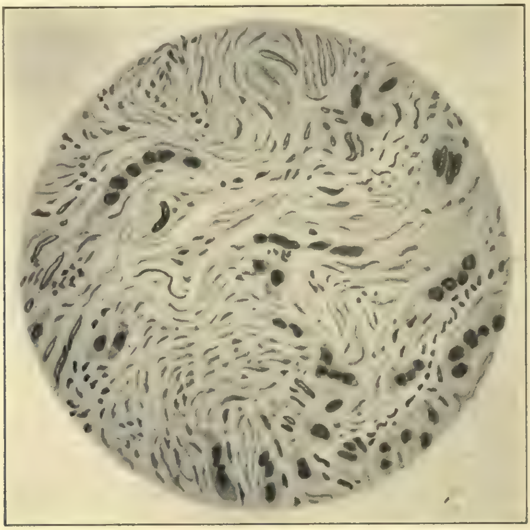

Fig. 85.—Uterine muscle one centimeter beneath the placental site. Postpartum (M.P.) Pregnancy hyperplasia of the muscle is still evident. Many dark cells with chromatin rich nuclei (chorionic wandering cells) are found lying between the muscle fibers. The appearance resembles that of a sarcoma of the uterus.

size is due to cloudy swelling, fatty changes and hyaline degeneration. Whether individual fibers perish is undetermined.

The thrombosed vessels are obliterated by hyaline degeneration of their musculature, and by endothelial proliferation. The other changes are alike in the subplacental decidua and the decidua vera. The separation has taken place in the glandular layer, carrying the superficial (toward the ovum) portion away with the placenta and membranes. The resulting raw surface is covered with fibrin and blood. The remains of the mucosa consist of decidual stroma (crowded apart by edema, interstitial hemorrhages) and thrombosed vessels, and the torn across fundi of glands. Before repair begins, a leucocytic wall is formed, superficial coagulation necrosis sets in, and a line of demarcation appears, just as in every granulating wound. The

glandular epithelium rapidly spreads, forming a new surface covering. The decidual stroma slowly returns to its connective tissue type. By the fourth week normal conditions are restored. Fetal elements are found deep in the uterine musculature, in the form of chorionic wandering cells, for seven to ten days post partum (Fig. 85).

The Lochia consists at first of red blood cells, fragments of decidua, leucocytes and epithelium. The red blood cells then hemolyze and appear as "shadows" (serous discharge). Fat droplets and bacteria abound, and gradually the fluid corresponds more and more to the secretion of any open wound.

D. Changes in the Adnexa.—The adnexa mechanically follow the uterus into the pelvis. The tubes rapidly become less succulent. Their musculature regresses.

In the ovary the corpus luteum of pregnancy shows advanced involutionary changes. Its center is already converted into connective tissue. By the third week it has regressed to the usual corpus albicans. By the second month follicle ripening is resumed.

Changes in the Vagina and Vulva.—Immediately after birth the overstretched tissues of the birth passages begin to regain their tonus. Macroscopic abrasions and minor injuries abound. The hymen is torn, and during its healing contracts to small tags—the carunculae myrtiformes.

The succulent surface epithelium and connective tissue slowly changes back to the resting type, and the vascular, especially the capillary net-work, diminishes.

Breast and other changes need be considered as during pregnancy an enormous proliferation of the glandular elements of the mamma has taken place.

After the products of conception have been expelled, the secretory activity begins. For a period, usually of three days, clear colostrum is obtained; after that, true milk is secreted.

The hypophysis, thyroid and *adrenals* return to their non-pregnant condition after shorter or longer periods. Symptoms due to hyperactivity of these glands in consequence disappear.

Physiology.—The factors which produce puerperal involution, are not at all understood.

A priori reasoning makes it evident that many of the changes constituting puerperal involutions are accounted for by the expulsion of the fetus and its placenta. The removal of this parasite not only does away with the demand for additional nutrition, but also explains the consequent contraction of the uterus, which mechanically obliterates many of the enlarged vascular channels. Most of the involutionary changes, therefore, are strictly comparable to those following the removal of a growth, a myoma, by enucleation, for instance. The other changes, however, are more specific and in all likelihood are due to the withdrawal of chemical substances, elaborated by the fetus and the placenta, which previously acted upon the

ovary and other glands of internal secretion. By the end of pregnancy, and probably long before term, the corpus luteum is a regressing gland devoid of function. Probably Halban is correct in assuming that the placenta acts as an inhibitory factor on breast secretion (l. c. 6). After the third stage mammary secretion can set in unchecked.

Definite observations dealing with return of ovulation after pregnancy are lacking in the human being. Records of isolated cases of impregnation immediately post partum are, however, extant. In the lower animals this period is most favorable for reimpregnation. Great variations are apparently the rule in women, as will be shown in the next paragraphs.

4. Lactation.—Nursing has a direct and appreciable effect on the female generative organs. In women who do not suckle their young, the process of involution is protracted and frequently incomplete.

The most striking phenomenon accompanying lactation is amenorrhea. The absence of menstruation is only relative. Approximately 50 per cent of nursing mothers begin to have regular periods two to four months after labor (26). Many women conceive anew during their time of amenorrhea.

On the other hand in a large number of women, nursing produces an extreme atrophy of the uterus—*lactation atrophy.* The reduction in size may be excessive, and if unduly prolonged, in rare instances, has led to permanent atrophy (27). During well-marked lactation atrophy temporary sterility probably obtains.

Nervous influences undoubtedly play some rôle during the first few days of the puerperium. Whenever the baby is nursed, strong contractions of the uterus occur, and are noticed by the patient. Whether these contractions continue, or influence the uterus after it has regressed, is uncertain.

Lactation probably influences ovulation, but to a variable degree in different individuals. No data concerning this fact are at hand. The uterus of lactation atrophy resembles the uterus before puberty in its smallness of size and lack of succulence. The absence of menstruation does not necessarily imply cessation of ovulation (vide ante). In the lower animals we have frequently noted regular estrus and conception during lactation (guinea pigs especially).

Recently certain investigators have ascribed an internal secretion to the mammary gland. If this proves to be true, though as yet no evidence has been adduced, the chemical action of the mamma might account for the changes mentioned.

It must also not be forgotten that amenorrhea is frequently due to constitutional causes (tuberculosis, diabetes, etc.). Perhaps nursing, which is a considerable drain on the entire organism, may act in a similar way. There is also a symptom complex depending on hypofunction of the hypophysis (Froelich's dystrophia adiposo genitalis) in which amenorrhea and genital atrophy are prominent. A hypophyseal origin must therefore, also be kept in mind, especially as the hypophyseal changes induced by pregnancy persists for many months.

This phase of sexual physiology has been barely touched. It should offer a fertile field for further investigation.

5. Senility.—*Symptoms of Menopause.*—With advancing age the period of reproductive activity gradually diminishes and finally ceases.

Usually no abrupt transition occurs, but a slow and progressive diminution of the cyclical phenomena takes place (28). Clinically we note that the menses become irregular, appear at longer intervals, and then definitely stop. Whether the cessation of menstruation always coincides with the cessation of ovarian activity is doubtful. Rare instances, in which gestation occurs many years after the apparent onset of the menopause speaks against this view. Numerous constitutional symptoms, ascribed to the absence of ovarian secretion, grouped under the appellation of "climacteric disturbances" are the rule. They embrace cardiovascular phenomena (flushes, palpitation, etc.), nervous disturbances (psychical, sensory, etc.), and protean manifestations of all kinds.

Anatomical Changes.—Gross. The local changes are due to progressive atrophy of the genitalia, and of the mammary glands. The vascularity of the parts diminishes, as the premenstrual engorgement and excitation ceases. The fundus of the uterus grows smaller and firmer. The infravaginal portion of the cervix constantly diminishes and in old age appears as a slight dimple in the apex of the conically contracted vagina (disappearance of the fornices).

The ovaries are reduced to hard, fibrous bodies. Finally they may be no larger than a bean.

The vagina and vulva lose their succulence and elasticity. The mucosa becomes harsh, dry, thin and readily injured. Consequently even slight traumata cause superficial defects, from which result synechial bands, obliterating the vagina more or less completely.

The mammary changes also consist of atrophy. The glands, therefore, become flabby, pendulous and small, unless fat accumulation prevents diminution of their size.

Microscopically.—The changes require but brief mention as they have been treated on page 38. The uterine muscle is largely replaced by connective tissue. The blood vessels show arteriosclerotic changes. The endometrium consists of a very thin layer, composed mainly of fibrous tissue, and contains a few straight glands. The surface epithelium may show scattered areas of squamous cells (metaplasia).

The ovaries on cross section appear fibrous. Few and imperfect ova are found (see Fig. 56, p. 65). Finally the organs are reduced to small masses of connective tissue within which run a few small vessels.

The vulvar and vaginal epithelium is diminished in thickness. Cornification and desquamation increase as the cervical secretion ceases. The submucous layer is thinner, more fibrous and less vascular. The elastic fibers are reduced in number.

The acinous structures of the breast disappear. Only the main ducts persist. The loose periglandular tissue is replaced by fibrous tissue. Irregular dilatations of the ducts are common.

Physiology.—No completely satisfactory explanation, accounting for the onset of the menopause has been offered. That the cessation of ovulation is due to exhaustion of the supply of ova is disproved by histological

evidence. Clark believes that the constantly increasing accumulation of scar tissue, resulting from corpora albicantia formation, and atresia of the follicles, finally prevents the expansion of growing follicles and stifles them at an early age. An interaction of other glands of internal secretion is more than likely. Probably the change is quantitative, a not sufficient number of follicles ripening to maintain nutrition.

The general atrophy of the other genitals is readily explained by the ovarian changes. It corresponds to the atrophy which follows castration.

CONCLUSIONS

We have attempted to trace the changes occurring in the genital tract from its earliest formation to old age, constantly contrasting clinical phenomena, anatomy and functional demands. Wherever possible we have described the forces which produce the functional variations, although our knowledge of their mode of action is still fragmentary. It must have become apparent to the reader that no successful mode of treatment can be evolved, that no clear conception of gynecological pathology can be obtained, unless these factors are known, understood and constantly borne in mind. Just as in other branches of medicine, *physiology* must always be made the basis of our knowledge, particularly if we aim to discover the innumerable influences exerted by the genital sphere upon the other organs of the body. Even in the most advanced female of to-day, we still find evidence—sometimes only vestigial, it is true—of the evolution from a primitive type, such as that of the queen bee, whose sole raison-d'être is that of reproduction. The perpetuation of the species is the goal in view during embryonic life and puberty. It influences the growth and development of the body, it calls to its aid the sex attraction, and never rests even after the goal is attained during maturity. Not until senescence makes further exercise of the essential function impossible do the genitals lose their importance in the body complex.

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CHAPTER V

THE VULVA

The vulva is a complicated region which partakes of the nature of ordinary skin, modified skin and real mucous membrane. It contains also the openings of various structures—the urethra, vagina, bartholinian glands, besides hair follicles, sebaceous and sweat glands. Therefore diseases of this region are varied and numerous.

Malformations of the vulva will be discussed in the chapter dealing with malformations of the entire genital tract.

I. SKIN DISEASES

Such diseases as are common to all integumentary regions must be studied in textbooks of dermatology. In passing, a few of the usual forms will be referred to.

Dermatitis, due to local or general causes is common (irritating discharges, douches). It merges with the various forms of vulvitis to be described.

Eczema and *intertrigo* especially in the diabetic, fat, and uncleanly.

Herpes zoster, commonest in premenstruum and in pregnancy.

Folliculitis and *furunculosis* in the debilitated, diabetic and uncleanly.

Diseases such as erythema, molluscum contagiosum (Goodall, 1), lichen, impetigo, psoriasis, offer no special features.

Nevi, angeiomata and condylomata, because of their importance in tumor diagnosis, are discussed in connection with vulvar neoplasms.

II. CIRCULATORY DISTURBANCES

Hyperemia is active when due to inflammations, *passive* in the venous stasis of decompensated heart lesions or of local pelvic pressure exerted by tumors or inflammatory masses.

Edema results from general causes such as heart and kidney diseases, from local causes in pressure produced by the pregnant uterus, pelvic tumors of neoplastic or inflammatory origin, and stasis in thrombosis of the pelvic veins as a sequel to puerperal septic conditions. Doughy or fluctuating enlargements of the labia majora result. These may attain large size and are subject to superficial irritation and to infection (erysipelas, phlegmons).

Varicosities are most commonly seen during pregnancy or, in multiparae as residua of previous pregnancies. Bulky convolutions of superficial dilated veins may assume the dimensions of real tumors. These varicosities may thrombose (Stolz, 2), as the result of trauma or infection. Rupture of a varix through direct violence (fall or kick), sudden excessive increase of venous pressure (cough, expulsive effort), or trauma during labor may cause serious hemorrhage.

Hematoma (or thrombus vulvae) is uncommon except during labor. Even under these conditions it occurs only once in from 2735 (Hirsch, 3) to 4000 (De Lee, 4) labors.

The resulting accumulations of blood in the non-pregnant are ordinarily small. They may rupture externally, or more commonly clot and are absorbed, in rare instances becoming infected and suppurating. Etiologically, to be considered are, rupture of varices of the labia, through cough or effort, direct injury from falls, blows (Hirsch, 3) (Van Cowenberghe, 5), violence sub coitu (especially in sexual aberrations), (Von Neugebauer, 6) or hemorrhage into bartholinian cysts (Veit, 7). In one instance a hematocolpos burst paravaginally into the labium (Bessler-Hagen, 8).

During labor spontaneous hematomata, not to speak of those resulting from pubiotomy, may reach great size, extending alongside the vagina, obliterating its lumen and causing dystocia. They may prove fatal from external hemorrhage after rupture (Roemer, 9), or internal bleeding, or if extending to the peritoneal reflection, may produce peritonitis when infected. Anatomically supra and subfacial hematomata are spoken of. If of large dimension, such hematomata always pass the limits of the vulva. (For literature see Lobenstine, 10; Hill, 11).

The writer has seen two cases of hematoma vulvae during labor. The one, of large size in the labium and extending upward along the vagina, burst spontaneously toward end of the second stage. The second case due apparently to meddlesome attempts to "soften the outlet of the vulva" increased at an alarming rate and caused arrest of the head at the introitus. It was therefore incised and evacuated and the vessels caught by suture after delivery. See also Pelvic Connective Tissues, Chapter XII, p. 439.

III. INJURIES

Most injuries of the vulva can be classified under three headings: accidental, coitus injuries and birth injuries (Royster, 12).

Severe falls, even upon blunt objects, may tear the labia, clitoris and bulb because the soft parts are pressed against the sharp rami of the ischium and pubis (Von Cowenberghe, 5). Impalements on fence pickets, pitchforks, cowhorns, etc., are on record (Bovée, 13), usually complicated by injury to other organs such as the rectum, vagina and peritoneum.

During coitus all grades of injuries from the slight physiological tear

of the hymen to complete tears of the perineum, complicated by tears higher up, result from rape committed against children, from abnormal practice, or more rarely from violent coitus in the case of old women with senile involution (Von Neugebauer, 6). Veit (15), in all cases of serious injury, believes that some unconfessed manipulations have been employed.

Injuries of the vulva during labor, unless insignificant in extent, are combined with vaginal tears. Purely vulvar tears, however, may prove serious at once because of hemorrhage, if the clitoris or its crura are torn, or later as a point of entry for infection to pathogenic organisms. The urethra or bartholinian duct may be torn (De Lee, 16), producing respectively urethral stricture and bartholinian cyst.

IV. INFLAMMATIONS (VULVITIS)

The vulva of adults is resistant to infection, except in the urethra and bartholinian glands, unless the epithelium has been previously softened by discharges coming from above. In children the delicate epithelium is more vulnerable. Vulvitis may be acute or chronic and may result from bacterial invasion, maceration by urine, or discharges and irritation by chemical or mechanical means.

1. **Gonorrheal Vulvitis.**—*In children* a severe acute gonorrheal vulvo-vaginitis is common. Hess (15a) found over 50 per cent of infants brought for admission to an infant's home, afflicted with vaginitis. A large number of cases are seen in dispensaries of cities. The contagion is spread by contact with contaminated towels, sponges, toilets, clinical thermometers. Epidemics occur in asylums and institutions. Occasional direct infection from adults, due to the superstition that contact with virgin genitalia will cure gonorrhea, are reported. Frankl (16a) finds the process limited to the infrahymenial structures in only 20 per cent; in 80 per cent he reports vaginitis. The bartholinian glands are rarely infected. Swelling of the labia, glairy discharge, excoriations and redness are noted. The gonococcus can be recovered from urethral and vaginal spread in the early stages. For literature see Gittings and Mitchell (16b).

In chronic conditions the vagina shows no lesions, the cervix alone being reddened and covered with mucopus. Hess (l. c. 15a) reports four autopsies which demonstrated the lesion of the cervix (redness of tip of cervix not extending into the canal, round cell infiltration of submucous tissue). When the vulvar and vaginal process has cleared up children may continue as "carriers" because of persistent gonorrheal cervicitis. Kiellberg Romanus (Dermat. Wochenschft, 1917, lxiv, No. 10) examined twenty women and girls who, as children, had had vulvo-vaginitis gonorrhoica. There were no present signs of the disease. Most of them were still too young to allow of conclusions as to sterility being drawn. It appears that the gonorrhea must cure itself or at least become latent, otherwise it would play some rôle

in girls of 12 to 18, and infection of the male at the first intercourse would be frequent.

Instances of systemic infections are not frequent (arthritis, Koplik, (17), peritonitis (Combey and Gadaud, 18).

In adults the process is most apparent in the urethra (acute urethritis, more rarely peri-urethral abscess, and infection of Skene's ducts), and in the *bartholinian glands.* A doughy tumor forms in the labium from closure of the main duct (pseudo-abscess). The duct epithelium is invaded by the gonococcus, leucocytic infiltration results and purulent secretion develops. The glandular alveoli are not affected. A mixed infection (staphylococcus aureus) may produce a real abscess with a granulation tissue wall, rupture through the labium and form a fistula.

The general labial redness, the discharge and the intertrigo result secondarily as the cervical leucorrhea continually macerates the vulva. At this stage gonococci are readily recovered from urethral or bartholinian pus.

Chronic gonorrheal vulvitis shows itself only on careful examination of the urethra (redness of Skene's ducts) of the reddened openings of the bartholinian glands (maculae gonorrhoicae). Bartholinian cysts are sterile, abscesses show no gonococci, and condylomata acuminata are often found in non-gonorrheal conditions. Gonococci may therefore not be obtainable in the vulva (then examine the cervical secretion). Gonorrheal vulvitis in the adult is almost invariably the result of sexual contact. With intact hymen I have seen it due to incomplete relations.

In children *agglutination of the labia* may result as a residuum of previous vulvitis, not necessarily, but usually gonorrheal in origin. If the small opening is posterior, drainage is satisfactory and the condition may escape notice until adult life. If the sole opening is anterior, stagnation of urine will arise early and produce irritative symptoms (Bokai, 19).

2. **Puerperal Vulvitis.**—Next in frequency is puerperal vulvitis resulting from infection of the numerous excoriations and injuries of the vulva following childbirth. Streptococci produce sloughy edematous ulcers covered with grayish exudate. The process may remain localized and produce gangrene, or extend, causing lymphangitis and bacteremia. Erysipelas may develop, spreading upon the mons and thighs. This is also seen in the newborn with streptococcic infections of the umbilicus. Milder infections result from staphylococci, bacillus coli, diphtheria bacilli, etc. The subject will be further discussed under puerperal infections (p. 480).

3. **Gangrenous Vulvitis and Noma.**

In severe infections either puerperal or occurring during the course of infectious diseases, often as a result of thrombosis, large areas of the vulva may undergo necrosis and slough off (Goth, 20). The infection may

prove fatal; if recovered from, scars, stenoses and deformities result. This condition is now extremely rare.

Noma is a gangrenous vulvitis occurring in debilitated children, more often in those living in institutions. It begins as a localized furuncle of the labium, rapidly spreads and often proves fatal (Blumer and MacFarlane, 21).

4. **Vulvitis during infectious diseases.**

During typhoid fever (Lartigau, 22), smallpox or vaccinia (Sloan, 23), scarlatina, diphtheria (Williams, 24), and dysentery vulvitis varying in severity from the catarrhal to gangrenous type may occur.

5. **Aphthous Vulvitis,** due to oïdium albicans, has been noted. It begins as a primary vaginitis, is found rarely in children but is common in diabetics and the aged (Littauer, 25).

6. **Non-specific Vulvitis,** simple vulvitis can be produced by diabetic urine, constant wetting from a vesicovaginal fistula, contamination from feces resulting from a complete perineal tear or rectovaginal fistula.

Discharges from above will produce like effects. Among the commoner causes producing the discharge are gonorrheal endocervicitis, carcinoma of cervix or gangrenous polypi and foreign bodies such as pessaries in the vagina.

Irritation due to masturbation, frequent violent coitus, oxyuris (thread worm), strong chemical douches (lysol) or chemicals applied locally, as iodoform, may produce acute vulvitis.

Actinomycosis.—A few cases have been reported (Lieblein, and Bongartz, Trapl (26). The infiltration, abscesses and fistulous tracts regularly associated with the disease are to be found. The pus contains the yellow granules characteristic of the ray fungus. In one instance pregnancy developed; cesarean section was necessary because of the vaginal infiltration (Trapl, l. c.). The prognosis is always very serious.

V. HYPERTROPHIC AND ULCERATIVE LESIONS

1. **Tuberculosis of the vulva** is rare. A tubercular primary lesion in the vulva has never been satisfactorily demonstrated, though Kroemer (27) regards his case as such. Most infections appear to be descending from the uterus and tubes (Von Baumgarten, 28), though a hematogenous origin cannot be excluded. Direct (Schenk, 29) and coitus infection has been claimed.

Nodular, ulcerative and hypertrophic forms have been described. Nodules are very rarely seen (Petit and Bender, 30), the vast majority of cases being first noted after breaking down has begun. The ulcers are serpiginous with sharply demarcated, irregular and undermined bluish edges. The base is dirty, granular and but slightly indurated. Small tubercles are found on the base and edges; cicatrization and advancement occur simultaneously. Widespread involvement of the labia, urethra, perineum and inner side

of the thighs may occur. Hypertrophic lesions are uncommon (Arndt, 31), but mixed lesions combining ulceration, hypertrophy, scar and fistulous formation have been described. Such lesions are difficult to distinguish from elephantiasis (Daniel, 32), or from esthiomène except when caseation, giant cells and tubercle bacilli in the tissues are found (Meriel, 33). Tubercle bacilli in the discharge are not decisive as these might have been carried down from a lesion higher up. Tuberculosis of the vulva has been noted in a child of two and one-half years (Karajan, 34), and in a woman of seventy-five (Logothetopulos, 35); it is commonest in early adult life. It may involve any or all vulvar structures. The inguinal glands are rarely affected.

2. **Syphilis of the Vulva.**—The manifestations include primary lesion, secondary efflorescences and gummatous masses. For details the reader is referred to books on dermatology.

The initial lesion may be a dry papule, an erosion or hunterian chancre. All three are characterized by induration, the last two also by loss of surface epithelium and presence of secretion. Histologically the infiltration zone is sharply demarcated from the surrounding tissue. It is composed of round and plasma cells, at first distributed only around the blood vessels (periarteritis) later also between them, and reaching to the epidermis. Giant cells and epitheloid cells are often found. Spirochetae pallidae can be obtained from the "irritation" serum as well as from the tissue.

Favorite sites of the initial lesion are the vestibule, fourchette and labium minus. On the labium majus a hard indurative edema (Taylor (36)), may develop. Multiple primary lesions have been described. When chancroidal infection has taken place a *mixed chancre* develops. With or without appropriate treatment the primary lesion heals, leaving first an indurated area and later a scar.

Condylomata Lata, the broad papule, are secondary manifestations. They appear as slightly elevated, disk-shaped lesions from pin point to size of a dime, often confluent and widespread, covering the entire vulvar and perianal region. The mass may become fungating and ulcerate. The epidermis is lacking in spots and a profuse, highly infectious thin saneous discharge containing the pale spirochete, is secreted. Microscopically there is a marked thickening of the malpighian layer, dense round-celled infiltration about the vessels and in the papillary layer an obliterating endartertis.

Tertiary lesions may evidence themselves as circumscribed gummata in the vicinity of the urethra, but more often appear as persistent ulcerations combined with edema and hypertrophy, thereby producing lesions difficult to distinguish from carcinoma, tuberculosis, elephantiasis or esthiomène (Gallagher, 37). The process may extend into the vagina and rectal strictures may exist coincidentally. Spirochetes are difficult to demonstrate.

3. **Ulcus Molle** (*soft chancre*) produces multiple ulcers (contact) of the labia. These may show rapid extension and produce widespread destruction (phagedenic ulcer). The Ducray strepto-bacillus is causative. Suppuration (bubo) of the inguinal glands is common. Ulcus molle may complicate a primary lesion (mixed) (Welander, 38; Goodman, H., 39).

4. **Esthiomène** (Ulcus Rodens) (ἐσθιό, to eat).

First described by Huguier (40) under the name of esthiomène and called ulcus rodens by Virchow, the process is characterized by a progressive slow ulceration which especially erodes the urethra and edge of the vagina. Widespread destruction, with hypertrophy resembling that of elephantiasis, (Stein and Heimann, 41) and partial cicatrization, produces a quite indescribable condition of distortion and disability (Fig. 86). Fistulae leading into the bladder and rectum, together with rectal strictures, continually

FIG. 86.—ESTHIOMÈNE. (Case of Dr. S. Pollitzer.) Deep destruction of posterior vaginal wall and fistulous tracts around rectum; patulous urethra.

keep up the irritation of the resulting cloaca. Esthiomène is resistant to both medication and operation and the prognosis is poor.

Tuberculosis and syphilis, which produce somewhat similar lesions, must be excluded. Microscopically the infiltrated ulcers often show giant cells (Pozzi, 42); Petit and Bender, 43), but have no special characteristics. Syphilis and gonorrhea together with marked general asthenia are said to be causative factors by reducing the resistance of the patient. The condition usually appears in prostitutes.

For literature see Murray (44), Schraeder (45), Koch (46), and Gunther (47).

5. **Elephantiasis Vulvae,** clinically consists of a thickening of the labia, clitoris or entire vulva. The resulting pale white, often pachy-

dermatous tumors, which may be pedunculated or sessile, may reach great size (Nicolas, 14 kg., 48), so as to hamper locomotion or cause dystocia (Green-Armitage, 49). The surface may be smooth (elephantiasis glabra), nodular (elephantiasis tuberosa), or diffusely warty (elephantiasis condylomatosa). While ulceration of the surface can develop secondarily, it is not essential to the process, as it is in tuberculosis, syphilis or esthiomène. Lymphorrhea may occur (49a).

The histology is by no means uniform. Dilatation of lymph vessels and edema are fairly constant, but the presence or absence of round cells and plasma cell infiltration, their distribution (perivascular, diffuse or aggregated), the occurrence of giant cells and epidermal changes, thickening or atrophy, are variable and inconstant (Croom, 50).

True elephantiasis is that of the Orient, due to the lymphstasis brought about by filaria sanguinis hominis (Bancrofti). In the Occident similar local stasis appears to follow the scars due to bubo or repeated attacks of erysipelas (Schmidlechner, 51). In many cases an antecedent history of syphilis can be obtained and rectal strictures may be present (Olshausen, 52). Antisyphilitic treatments are of little or no value. It seems as erroneous to classify elephantiasis as a syphilitic lesion as Hurdon (53) has done, as to cell it a tubercular process (Forgue and Massabuau, 54). The disease as found in the Southern United States among the negroes resembles the Oriental type (Hill, 55).

Cases of special interest are those of Heil (56), Traina and Marconi (57), and Chrobak (58).

Differential Diagnosis.—From what precedes it will be seen that clinically tuberculosis, syphilis, esthiomène and elephantiasis may produce lesions difficult to differentiate. The combination of ulceration, hypertrophy and healing, complicated by the secondary changes induced by factors such as incontinence of urine and leakage of feces resulting from fistulae, account for the confusion. By finding tubercle bacilli and spirochetes (or typically periarterial infiltrations) tuberculosis or syphilis can be classified. Esthiomène is mainly ulcerative, elephantiasis mainly hypertrophic, but combinations of the processes have been described (Stein and Heimann, l. c.). Neither have sufficiently characteristic histological criteria to permit of absolute classification by the microscope.

6. **Condylomata Acuminata** (venereal warts), are multiple soft warty excrescences which occur on the labia but may encroach upon the thigh and perianal region, and especially during pregnancy invade the vulva (Traina and Marconi, 57) (Fig. 87). Although commonest as a sequel to gonorrhea, they are not necessarily venereal, resulting as well from irritation of non-specific nature, so that they may be found in children and virgins (R. R. Smith, 60). A certain degree of contagiousness is ascribed to them. Possibly this is due to the acrid discharge which is loaded with bacteria and various types of spirochetes (Ewing, 61).

FIG. 87.—CONDYLOMATA ACUMINATA OF VULVA IN PREGNANCY. Large soft warty growths projecting from vagina and vulva. In this case the cervix also showed condylomatous growths.

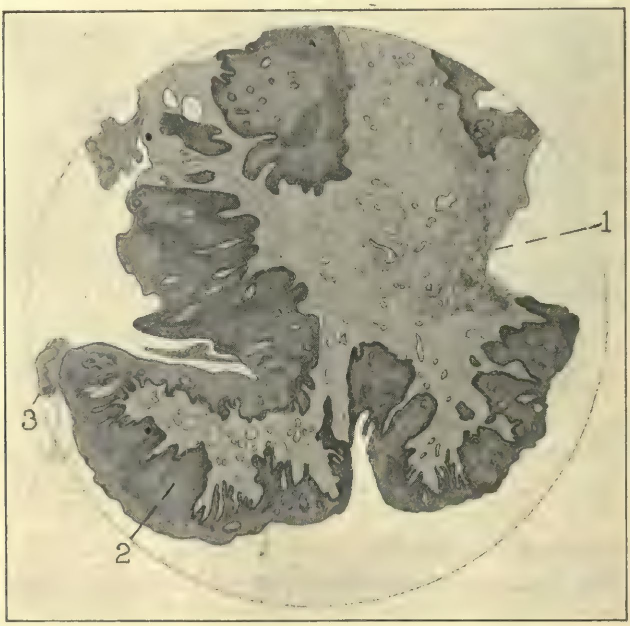

FIG. 88.—CONDYLOMATA ACUMINATA OF VULVA. (L.P.) Wart like excresence, with many clefts, composed of hypertrophic squamous epithelium on a frame work of loose vascular connective tissue. Denuded areas without epithelial covering allow profuse escape of secretion. 1. Denuded area. 2. Squamous epithelium. 3. Exudate adherent to surface.

The warts are due to an inflammatory hypertrophy of the papillary layer and marked thickening of the overlying epithelium which is imperfectly hornified. Thus are produced slender, branched, warty growths. Their stroma is vascular and often infiltrated. An acrid secretion exudes from areas denuded of epithelium (Fig. 88).

VI. ATROPHIC AND ALLIED LESIONS

Pruritus vulvae, kraurosis and leukoplakia have frequently been confounded. This is largely because pruritus, which in most cases is merely a symptom (itching), may be present in both kraurosis and leukoplakia, and because leukoplakia has often been seen in combination with kraurosis.

1. **Pruritus,** or chronic itching of the vulva, is usually the result of irritation (sweat, urine, leucorrhea, congestion, lack of cleanliness, etc.). "Essential pruritus has been classified as a neurosis (Webster, 62). Its existence is more than doubtful. In connection with pruritus secondary changes, such as scratch marks, leathery thickening and loss of gloss are described. The itching, however produced, causes scratching, and the mechanical irritation not only increases the itching but also produces the objective changes just mentioned. Veit (63) considers the process a para-keratosis due to inflammation, and pictures it (Fig. 6, p. 596) as a subepithelial round-celled infiltration and irregular desquamation of the hornified layers.

It cannot be denied that pruritus in many cases precedes and accompanies kraurosis, and very probably the chronic irritation may be the same in both diseases, but on the other hand, many cases of kraurosis do not complain of itching (Trespe, 64).

2. **Kraurosis** is an atrophy of the vulva due mainly to cirrhosis of the subepithelial constituents of the skin. Although a disease commonest in the senium, it has been observed in the young (Rosenstein (65)). In the typical case the labia majora flatten out, the small labia completely disappear, mere indications of the clitoris and prepuce are found and the vulvar orifice contracts so as to barely admit the tip of the finger. The urethra is usually distorted and patulous. In extreme instances, the adjacent skin of the thighs and the perineum are involved. Early in the disease, or in some cases throughout its course, one or other of the components of the vulva may be unaffected, the process may be unilateral (Fleischmann, 66), or contraction of the vulvar orifice may be absent (Veit, 67), although Breisky (68), who originally described kraurosis, considered this the essential lesion (*κραυρόω*, to contract). The surface of the vulva looks thin, glistening, tense, dry and whitish. Pigment atrophy and disappearance of all hair,

together with the tension of the parts are striking. Excoriations and cracks result from the scratching and brittleness.

Histologically characteristic are the changes in the corium. The papillae are low or effaced, the connective tissue is atrophic and scarry, and round and plasma cell infiltrations are present to a variable degree. Sweat and sebaceous glands, hair follicles, vessels and nerve endings are either atrophic and diminished in number or absent (Fig. 89). Epithelial changes are inconstant, the malpighian layer often being reduced in thickness (Breisky, l. c. 68, Berkley, 69).

The etiology is unclear. Veit considers pruritus as the prekraurotic disease and kraurosis as the end product of a chronic inflammation (p. 620). Trespe (64) found 50 per cent of the cases had never suffered from pruritus. Jayle (70) considers atrophy of the ovaries a factor, and Schickele and also Gellhorn (71) report cures by exhibition of ovarian extracts. Doubtless the nutrition of the parts is reduced, especially after the

FIG. 89.—KRAUROSIS VULVAE. (M.P.) (Specimen of Dr. F. S. Mandlebaum's). The epidermis is shrunken and hard. The papillae are smoothed out and the connective tissue is shrunken and degenerated. Round-cell infiltration is marked throughout. Few vessels and these with narrow lumina. Contrast with Fig. 90.

climacterium, but ovarian insufficiency (spontaneous or after operative ablation) is so frequent and kraurosis so uncommon that this causal connection becomes most unlikely. Carcinoma as end result of kraurosis has been repeatedly observed (Brettauer (72), Trespe, 64; Rosenfeld, 73), though less frequent than as a sequel to leukoplakia. Without excision kraurosis advances to an intolerable degree (itching, incontinence of urine, tension), and the hazard of cancer increases proportionally.

3. **Leukoplakia,** which is not an atrophy of the skin, is considered in this connection merely because of its intimate relation to pruritus and kraurosis. The disease was first described by Weir (74), since then its relation to cancer has been confirmed more and more.

White, thickened, non-transparent patches, described as asbestoslike, appear on the labia majora or other parts of the vulva or even upon the skin of the thighs. They are the result of hyperkeratosis, a thickening of the stratum lucidum and cornium, oftener accompanied by some round-celled infiltrations of the papillary portion of the corium (Fig. 114 under Vagina) (Pichevin and Petit, 75).

Leukoplakia results from prolonged chronic irritation in this location (just as it does in the mouth), but appears much less often as a direct sequel to syphilis (in the mouth in 70 per cent according to Erb (76). Veit (77) states that leukoplakia is but very rarely absent in cases of carcinoma of the vulva except in those originating from glandular structures (bartholinian, etc.). Leukoplakia may therefore be regarded as a "precancerous lesion" if we limit the meaning of this misleading term to that, the disease is "merely observed to precede and favor the development of cancer" (Ewing, l. c. 61, 459).

VII. CYSTS OF THE VULVA

These formations are neither of great clinical importance or of much pathological interest. The majority are retention cysts.

1. **Cysts of the Bartholinian Gland.**—*Classification.*—Cysts of the bartholinian glands are classified (Huguier, 78) as gland or duct cysts. The duct cysts are oval and situated in the lower third of the labium majus; the gland cysts are globular and more deeply placed, extending alongside the vagina or backward toward the rectum. Both varieties result from closure of the duct after inflammation, most often, but not necessarily (Wiener, 79), of gonorrheal origin. The pus in time becomes sterile and the contents is then glairy and clear, turbid or bloody. Not infrequently an unnoticed retention cyst will show an exacerbation of the chronic inflammation and may even produce a labial phlegmon, and after rupture, leave a permanently secreting labial fistula. The cysts, usually the size of a plum, may exceptionally reach the dimension of an adult fist. The cyst lining is composed of transitional epithelium, sometimes of cylindrical or cuboidal epithelium. Frequently parts of the more or less altered gland lobuli are found in the wall (Cullen, 80).

Coen (81) described an adenoma of the gland. Scott (82) found concretions in a cyst. Carcinoma of the gland will be described in a succeeding paragraph.

2. **Sebaceous cysts** are found not infrequently on the labia majora, minora or the prepuce (Fig. 90). They are like wens on the skin surface, being lined with stratified squamous epithelium and having a pultaceous contents. They may become infected. *Epidermoid cysts* are similar except that they are derived from congenital fetal remains, or due to inclusions of skin from small traumata or operative interference (Simon, 83).

3. **Hymenal cysts,** which are of varied derivation, occur either along the edge, or median part of the vestibular surface. They have been ascribed to coalescence of hymenal folds (Döderlein, 84), to retention cysts of sebaceous or mucoid glands occasionally found in the hymen (Bastelberger, 85), or to fetal remains derived from Gärtner's duct (Palm, 86).

4. **Lymphangiomatous "cysts"** of small size due to dilatation of lymph vessels (Piering, 87).

5. **Mucoid cysts** from closure of the widely distributed mucoid glands, especially in the vestibular region.

6. **Papilliferous cysts** (Gebhard, Bondi, 88) often with ciliated epithelium.

7. **Adenocystoma papilliferum polyposum** (Pick, 89), a cyst filled with dense papilliferous projections covered with cuboidal, cylindrical and squamous epithelium.

8. **Hidradenoma and adenoma hidradenoides** (Pick, 89). Small subcutaneous or pedunculated polycystic tumors, whitish in color, derived from sweat glands (Pick, 90). The alveoli have a double layer of epithelium and a well defined membrana propria. Direct con-

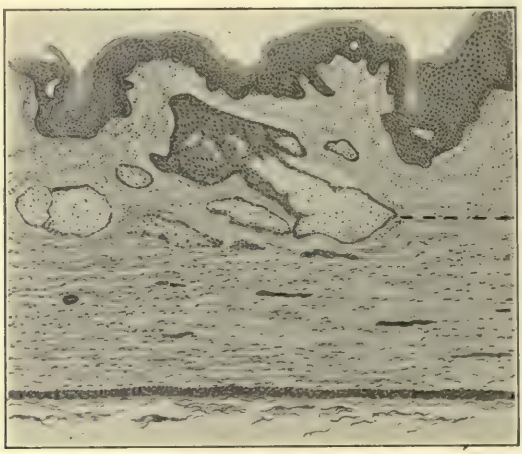

FIG. 90.—SEBACEOUS CYST OF LABIUM. (M.P.) Labium is normal but harbors a sebaceous cyst. Contrast with Kraurosis (Fig. 89). 1. Epidermis. 2. Sebaceous gland of labium. 3. Connective tissue. 4. Epithelial wall of sebaceous cyst.

nection with a sweat gland or with its excretory duct can often be shown. Kaufman (91) warns against mistaking a metastatic adenocarcinoma, which histologically has a superficial resemblance, for this type of growth.

9. **Cysts secondarily becoming vulvar,** i.e., advancing by extension or growth into the vulva.

A. **Cysts of canal of Nuck** (hydrocele muliebris), a cystic dilatation of the closed-off end of the sac of an inguinal hernia (Clark, 92). The wall is composed of fibrous tissue and possibly striped and unstriped muscle. There may be a low cuboidal or cylindrical epithelium (peritoneal endothelium) or this may be lacking. Occasionally simple glandlike structures may be found in the wall (peritoneal glands—see Fig. 153). The cyst develops in the upper half of the big labium with a subcutaneous pedicle leading to the inguinal canal.

B. **Gärtner's cyst of vagina enlarging into labium** (see p. 146).
C. **Cystic dilatation of the end of an accessory ureter.**

VIII. BENIGN TUMORS OF VULVA

1. **Lipoma** of the vulva may be sessile or pedunculated and usually appears in the mons or labia majora. Temporary fluctuation in size during menstruation and pregnancy has been noted. Connection with the subperitoneal fat by means of a paravaginal pedicle is a rare condition (Headly, 93; Graefe, 94).

FIG. 91.—LIPOMA OF VULVA. (L.P.) The fine septa represent cell boundaries between individual fat cells. The coarse septa are connective tissue binding the tumor into lobules. The fatty material has been extracted during the preparations of the section, hence the empty honeycomb spaces.

Lipomata are usually encapsulated and consist of pure fat tissue (Fig. 91).

Quenu (95) describes a congenital lipoma in a child five months old.

2. **Fibroma** and **fibromyoma** of the vulva may originate from the connective tissue of the labia, from the pelvic fascia and from the terminal portion of the round ligaments (see p. 441). These tumors are sessile or pedunculated, hard, lobulated and, when edematous, occasionally semifluctuating. They may reach great size (Géroulanos (96), growth weighing 8 kg.).

Fibromas are composed of connective tissue, either of closely woven adult type (fibroma durum), or edematous and finely fibrillar (fibroma molle, Fig. 92).

FIG. 92.—FIBROMA MOLLE OF LABIUM. (L.P.) Fibrillar connective tissue amid which numerous capillary blood vessels show as darker areas, studded with the nuclei of their endothelial cells.

FIG. 93.—ANGIOMA. (L.P.) Small tumor of labium composed of numerous cavernous vessels surrounded by a sheath of small cells. The surface is covered with normal epithelium. The little tumor histologically bears a strong resemblance to the primary lesion of syphilis.

Fibromyomata in addition contain unstriped muscle tissue. Those derived from the round ligament may contain epithelial inclusions variously interpreted as peritoneal glands or wolffian derivatives. (Emanuel, 97). Hyaline degeneration (Piering, 98), cavernous vascularity (Dienst, 99) and calcification of fibromata are reported. For classification and literature see Leonard (100). This author claims that one-fifth of all cases become sarcomatous (?).

3. **Angioma** in this region does not differ from those of the general skin surface (Fig. 93). Hemangioma capillare (Figs. 94A and 94B) and lymphangioma (Jayle and Bender, Brindeau, 101) are on record.

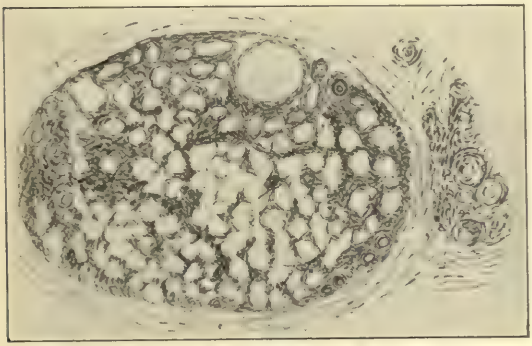

FIG. 94A.

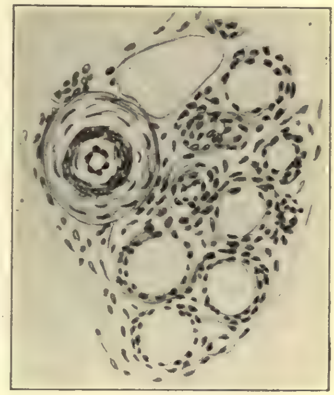

FIG. 94B.

FIG. 94A.—HEMANGIOMA CAPILLARE OF VULVA. (L.P.) This tumor bears a superficial resemblance to the frame work of an alveolar carcinoma in which the epithelial cells have dropped out.

FIG. 94B.—HIGH POWER OF FIG. 94A SHOWS THE VASCULAR LUMINA WHICH ARE SURROUNDED BY SMALL ROUND CELLS.

4. **Mixed Tumors and Teratomata.**—Here too the casuistic is small. Enchondromata of the clitoris have been described, but all three cases without microscopical report. *Fromme* (102) removed an encapsulated fibroma containing glands, fat and myxomatous tissue. Duclaux and Herrenschmidt (103) evidently had to deal with a true teratoma containing among the constituents intestinal mucosa. Fisher (102a) removed a typical primary myxoma with some included glandular structures and slight round-celled infiltration at the periphery. Ley (102b) ablated an ulcerating mass from a five-weeks-old child. The pedicle involved the urethra. Unstriped and striped muscle, the latter largely of early embryonic type, and nervous tissue composed the "teratoblastoma."

5. Closely allied to real neoplasms are urethral caruncles.

Urethral Caruncles are small (pea-sized) bright red sessile or pedunculated growths, projecting from the mouth of the urethra or depend-

ing from its posterior edge. These tumors are highly sensitive. They may be combined with prolapse of the urethral mucosa. Caruncles are of various structure. Most of them will fall into one of three classes Williamson and Atlee, 104).

1. *Granulomatous,* which show round-cell infiltration and thrombosis of vessels and unchanged squamous surface epithelium (Fig. 95), apparently not true neoplasms, but the result of chronic urethritis. 2. *Papillary*

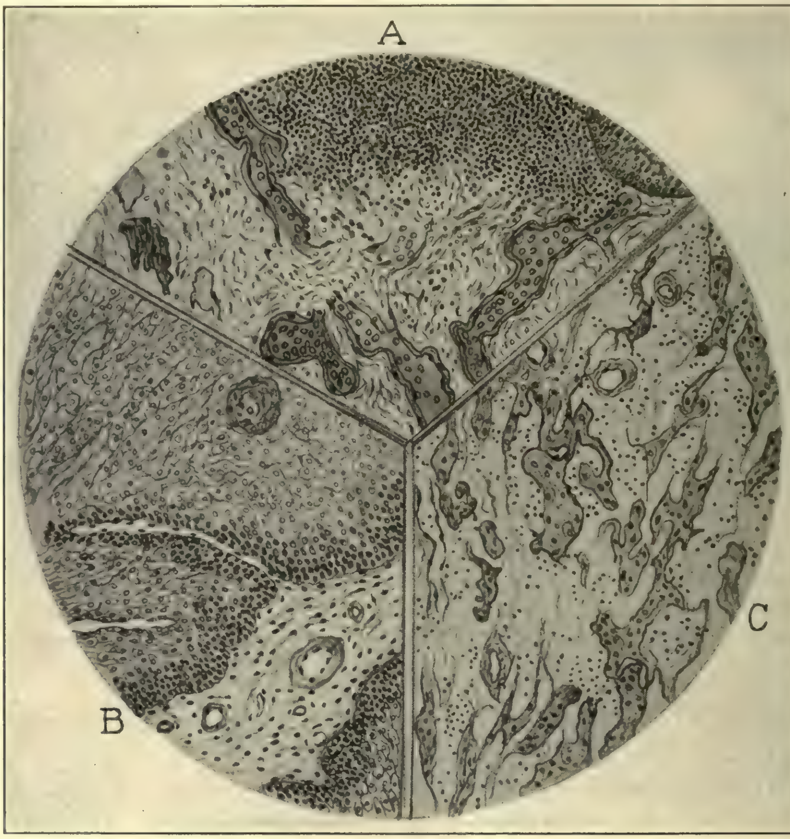

FIG. 95.—URETHRAL CARUNCLES. (M.P.) A. Granulomatous tissue with round-celled infiltration, thrombosed vessels. B. Papillary angiomatous, resembling wart. C. Telangiectatic.

angiomatous, due to proliferation of surface epithelium with vascular stroma and often containing tubular glands (Fig. 95B). 3. *Telangiectatic,* showing dilated blood vessels and unaltered surface covering (Fig. 95C).

In children caruncles do not occur, according to Stoeckel (Veit's Handbuch, Vol. II, page 315), cases reported as such being prolapses (105). While this rule is not absolute, caruncles most frequently appear toward the end of the period of sexual activity.

Pure myoma of the urethra has been described (Büttner, 106), also *fibromyoma of urethra* (Kretschmer, 107), of urethrovaginal septum (Coe, 108), and *adenoma* of urethral opening (Spencer, 109).

6. Finally nevi will be referred to, as in many instances melanotic carcinomata or sarcomata take their origin from these benign growths.

Nevi are usually small, congenital tumors, either flattened or elevated, which, in the majority of instances, are pigmented. They form hard or soft pigmented warts. The typical nevus contains strands of clear cells in acellular stroma (Fig. 97, nevus verrucosus). These cells are referred by some (Ribbert, 110) to a mesodermal origin, by others are regarded as epithelial (Kromeyer, 111).

An impartial and full account of the opinions held and the facts upon which they are based will be found in Ewing's book (112).

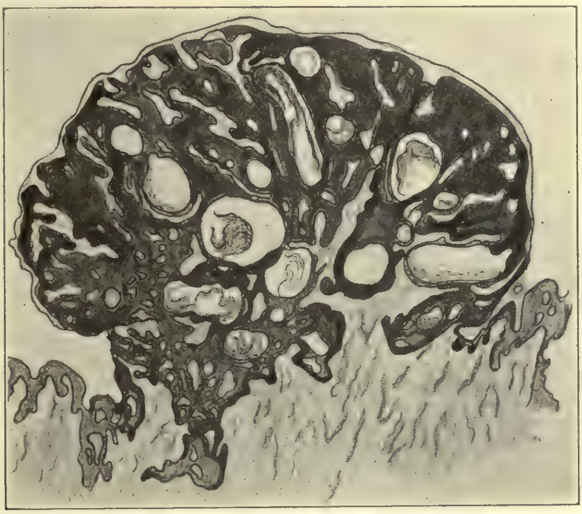

Fig. 96.—Pigmented horny wart. (V.L.P.) Bears superficial resemblance to melanoma. Shows no infiltrative tendency, nonmalignant.

The pigment may be the striking feature, a horny pigmented wart (Fig. 96) giving a most malignant impression under the microscope though benign (Fig. 97).

These warty growths in response to trauma, irritation or unknown stimuli, may suddenly become malignant, giving rise to melanotic tumors, histologically carcinoma, sarcoma or transitions containing both.

Favera's (113) article contains a good résumé of the literature.

IX. MALIGNANT TUMORS OF THE VULVA

1. **Carcinoma of the Vulva,** according to Schottländer (114), represents from 2 to 4 per cent of genital cancer. Ewing places the incidence

at 10 per cent, apparently basing his views on the old statistics of Gurlt (115).

The patients are usually over 50 years of age, in Von Winckel's (116) statistics 64.5 per cent having passed that age. However Kinoshito (117) observed cancer of the vulva in a girl of fifteen years and Arnot (118) in a patient of twenty. The sites of occurrence are, in order of frequency, the labium majus or the interlabial fold, the clitoris. urethra, other parts of the vulva and most rarely the bartholinian gland or duct.

FIG. 97.—SIMPLE NEVUS VERRUCOSUS. (M.P.) Shows strands of "nevus cells" which bear close resemblance to epithelial cells of cancer. Absence of mitoses and of polymorphism are striking.

As mentioned under pruritus, kraurosis and especially leukoplakia, these conditions in many instances appear to precede and perhaps to favor the incidence of cancer (Weir, 119). Antecedent to the appearance of cancer, a thickened fissured epidermis, or localized papule or wart may have been noted. The carcinoma develops in one of three forms, a diffuse, hard infiltration, gradually invading the entire vulva (Fig. 98); cauliflower growths (Fig. 99), but most commonly the indurated ulcer (Fig. 100). Early involvement of the inguinal lymph nodes appears characteristic, Dittrich (120) finding 50 per cent involved within the first year, Rupprecht (121) 100 per cent within that

time. Enlargement of the glands may be due to infection resulting from the ulceration. Of the enlarged glands examined by Schwarz (122), less than one-half (five out of eleven cases) were cancerous.

Vulvar carcinoma is notorious for its malignancy and frequency of recurrence after operation. Early ulceration, wide infiltration or para-urethral and vaginal tissue, involvement of the pubic and ischial rami, are the rule. Death from hemorrhage, after erosion of the common femoral artery by carcinomatous inguinal glands is not uncommon.

FIG. 98.—DIFFUSE CARCINOMA OF VULVA. Showing infiltration and ulceration.

In advanced cases metastatic foci on the abdominal wall, extension to the thighs and profuse suppuration (often thrombosis of the femoral vein occurs), cause profound cachexia. Death may occur in from a few months to two years. General metastases are rare.

Implantation by contact on the opposite labium has been reported. Kehrer (123) collected thirty-five of these cases, Dittrich, however, ascribing the condition to discontinuous lymphatic involvement, which is more in accordance with our present conceptions.

Metastatic carcinoma (124) of the vulva is not uncommon, the primary focus being in the ovary, or uterus. After vaginal hysterec-

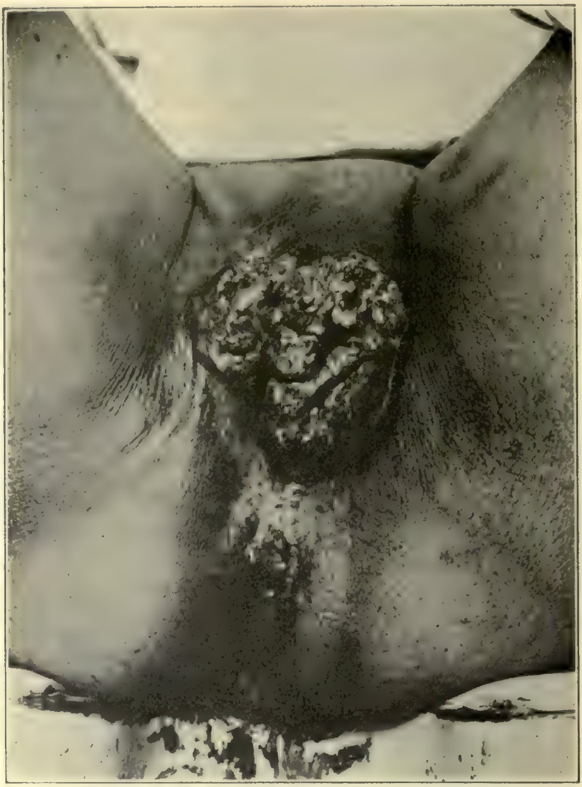

FIG. 99.—CARCINOMA OF VULVA. Cauliflower growth with marked breaking down.

FIG. 100.—CANCER OF CLITORIS. Small indurative ulcer. In a woman aged sixty, inguina glands already enlarged.

tomy direct implantation is often seen in the scar of a paravaginal incision (Amann, 125).

Primary vulvar cancer recurs in a large percentage of cases after operation. The reports vary anywhere from between 7 to 25 per cent of cures after a period of five years (126). With the more radical removal of glands, especially intrapelvic glands (Stoeckel, 127), better results may be hoped for. Repeated operations for recurrences may prolong life for years (Fraenkel (128), three operations, death after 24 years).

FIG. 101.—CARCINOMA OF CLITORIS. (L.P.) At the left upper edge, normal surface epithelium gradually showing invasion downward, with little apparent change in type. Below, areas with pearl formation. Throughout considerable round-cell infiltration.

The majority of vulvar carcinomata are squamous epitheliomata in solid masses or long cords. Both undifferentiated and adult types, either basal cell or with hornification and pearl formation are encountered (Figs. 101 and 102). Adenocarcinoma occurs rarely in the bartholinian glands, and still more rarely in the urethra. Other adenocarcinomata in the vulvar region are almost invariably metastatic, except the adenocarcinoma hidradenoides derived from sweat glands, and an occasional clitoris tumor (v. Engelhardt, 129). Melano carcinoma will be described separately.

The casuistic of *clitoris carcinoma* has been collected by Basset (130), who found 147 cases, many associated with leukoplakia. Of cancer of the bartholinian gland about twenty in all have been reported. For literature see Veit (131), Fabricius (132), Spencer (133). These were adenocarcinomata except in Sitzenfrey's (134) case, which was a squamous epithelioma with hornification.

Urethral carcinoma is very rare, if tumors secondarily growing about the urethra and immobilizing it, are excluded (Whitehouse, 134a). McMurtry, in 1908, collected 26 cases (134b). Primarily urethral cancers take origin from the mucosa, preferably extend intraurethrally as ulcerating, superficial, often papillary tumors toward the bladder neck (Mais, 20 cases (135). I have observed one such case, in a woman of seventy, in which the

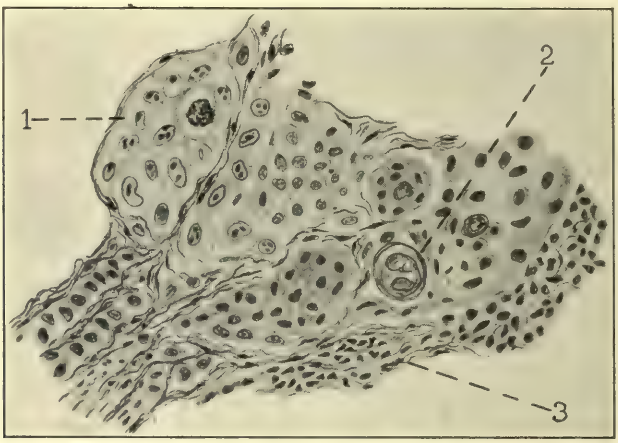

FIG. 102.—CARCINOMA OF VULVA. (M.P.) Showing alveolar arrangement, squamous form and melanomatous transitions resembling sarcoma. 1. Alveolar distribution. Note giant mitotic figure. 2. Squamous, with pearl formation. 3. Melanotic portion showing below almost connective tissuelike cells, above merging with squamous.

tumor finally invaded the bladder. Vulvo-urethral (Heinsius, 69 cases, 136), origin, that is arising from the junction point of these two structures are most frequent, and cancer arising from meatal polypi, (Puppel (137), adenocarcinoma), are also recognized. For reference to literature see Watson (138). *Sweat gland adenocarcinoma* of which only two cases are on record (Ruge and Schiffmann, 139), appear to evince very slight or no malignancy.

Carcinoma of the hymen is described by Frankl (139a) in a virgo of fifty-seven. The tumor was of glandular type.

DIFFERENTIAL DIAGNOSIS

The diagnosis of carcinoma should, of course, be confirmed by the microscope. In the vulvar region ulcerating, tubercular, elephantiastic and neglected syphilitic lesions, esthiomène and occasionally irritated

condylomata and nevi may be submitted for diagnosis. With modern methods of animal inoculation and newer cultural technic, tubercle bacilli and spirochetes should be found when present. Carcinoma can be diagnosed by its histology. This will leave only esthiomène and elephantiasis, in which the criteria are not absolute. Possibly further research will eventually enable us to docket these anomalous symptom complexes among already well-defined diseases (Tbc., lues).

2. **Sarcoma of the Vulva.**—Sarcoma of the vulva is very rare. O. Frankl (140) places them at 0.01 per cent, inclusive of melanoma (no authority or statistics given). These tumors appear earlier than carcinoma, one-half of the patients being below forty years (141). In Bluhm's (142) case the patient was twenty-one years old.

Sarcomata occur mainly on the labia, the clitoris and urethra. They resemble fibromata until ulceration and infiltration takes place. The tumor may be sessile or pedunculated and may attain large size (v. Winckel (143), pedunculated mass, size an adult head, round-cell sarcoma). Early tendency to recurrence is the rule and multiple metastases may develop. The lymphatic glands are rarely affected, thus differing from carcinoma and melanoma.

The histology is varied, myxosarcoma (Hunter Robb (144), Watson, 138), spindle (Hartman, 145), and fibro sarcoma (Caruso, 146), being most frequent. Polymorphous (Francke, 147), round-celled (Winckel, 143), endothelial (Delle Chiage, 148), giant-cell (Szili, 149), and perithelial (Schmidlechner, 150) forms have been described. (Of twenty-six cases—ten myxo, four fibro, six spindle, three polymorphous; one each, endothelial, perithelial and angeiomatous.)

Sarcoma of the round ligament is reported by Maly (151).

Sarcoma of urethra (Nebesky (152) 15 cases from mucous membrane, three from muscle wall; Flatau (153) with inguinal gland involvement).

Sarcoma developed on fibroma, Lichtenstein (154).

Sarcoma developed on elephantiasis, Chrobak (155).

Sarcoma of bartholinian gland, Bluhm (142), Hofmeier (156).

For literature see Veit, l. c. 7, ii, 741.

3. **Melanoma of the Vulva.**—The majority of these growths have been published in the literature as melano sarcomata. Their histogenesis is so doubtful that the writer prefers to classify them separately. See Nevus, page 119. They are rare growths, but more common than sarcomata. They usually appear on the labia or clitoris as bluish, black or merely dark sessile tumors. Pedunculated growths have been reported by Ferguson (157) and by Lockhart (158). A very rapidly fatal course marked by ulceration, lymph gland involvement and occasionally the

most widespread metastases (including multiple cutaneous ones), makes melanoma of the vulva a nearly hopeless disease.

Out of the literature Veit (iv, ii, 748) was able to find only four cures of which two were of comparatively short duration. Hirst (159) reports a case with hyperacute course in which the tumor developed while the patient was in the maternity hospital, death from general metastases resulting in four weeks. Where lymph gland instead of vascular dissemination is prominent, a less malignant course may be run. P. Meyer (160) permanent cure after removal of three recurrences; S. Fisher (161) after removal of involved inguinal glands several years after the primary operation.

The age incidence is later than in sarcoma but earlier than in carcinoma (of twenty cases, four were below fifty, eleven between fifty and seventy, and three above seventy years).

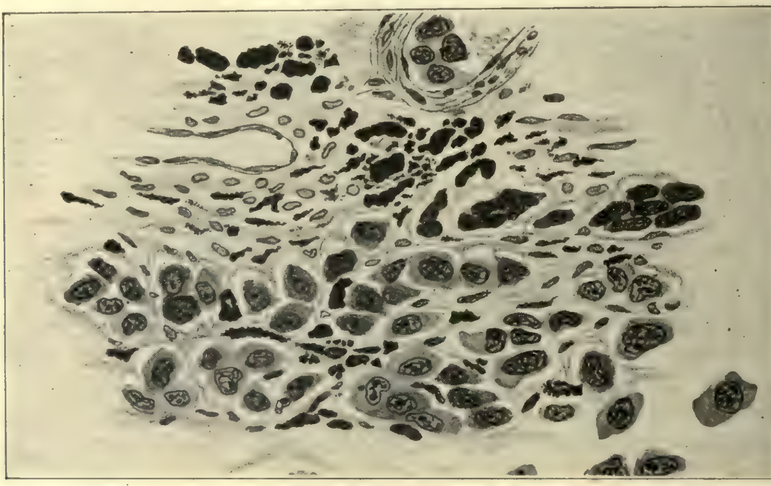

FIG. 103.—MELANOMA OF VULVA. (H.P.) Sarcomatous in type, showing mainly intracellular pigment. Above, capillary vessel containing tumor and red blood cells.

The morphology of melanoma is variable. It may appear as a pigmented alveolar sarcoma (Fig. 103), as a carcinoma with pearl formation (Fig. 104) which may show all histological transitions to sarcoma. The pigment may be scant or excessive in amount, extra- and intracellular. The metastases may be alveolar carcinoma, or spindle-cell sarcoma, perithelioma or prove lymphosarcomatous in type, and may or may not contain pigment (Ewing, l. c. 61, page 856).

For details of the scanty literature see Veit (4, ii, 745). Rothschild, (126) has collected 57 cases.

Vulvar metastases of chorionepithelioma and hypernephroma (Graefenberg, 162) are recorded. The writer saw a case of the latter (unpublished case of Dr. A. G. Gerster, Fig. 105).

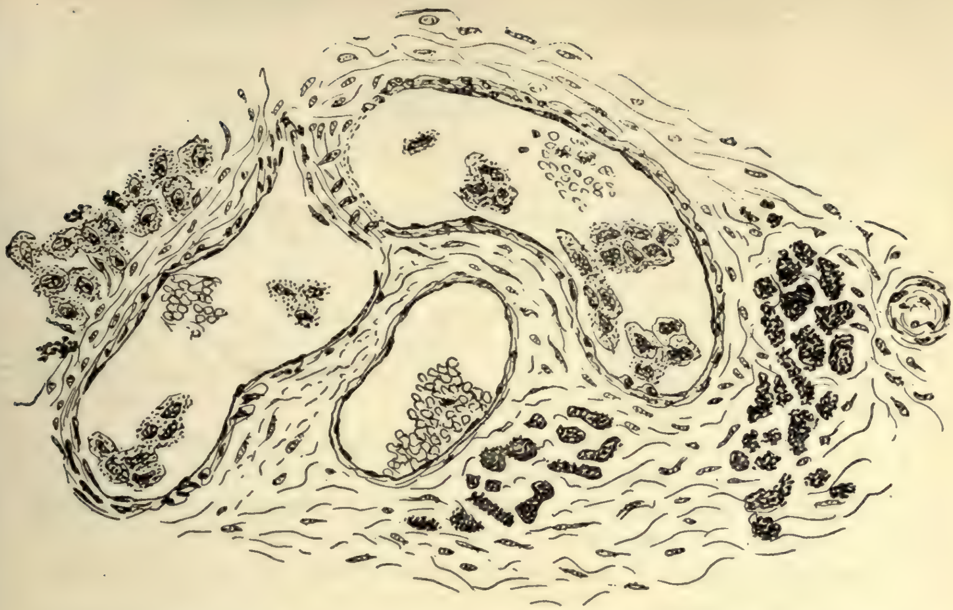

FIG. 104.—MELANOMA OF VULVA. Showing vascular tissue resembling angio-sarcoma. In vessel lumen numerous cells loaded with pigment. To right, deeply pigmented connective tissue cells. To left, and above, epithelial cells, likewise loaded with pigment.

FIG. 105.—METASTATIC HYPERNEPHROMA. Appearing three months after nephrectomy. (Unpublished case of Dr. Arpad G. Gerster.)

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1904	Jacoby	40 cases	25% cured.	Monatschr. f. Geburtsh. u. Gynäk. 1904. 19:365.
1912	Rupprecht	25 cases	24% cured.	L. c. (121).
1912	Kehrer	200 cases	7% cured.	L. c. (123).
1912	Taussig	114 cases	12% cured.	Interst. Med. Jour. 1912. Dec.
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		84 cases	9.5% cured with gland removal.	

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CHAPTER VI

THE VAGINA

I. INJURIES

The causes producing injuries of the vagina, in the main, are identical with those mentioned under vulvar injuries—trauma, coitus and parturition. In addition, injuries due to the presence of foreign bodies must be considered.

1. **External Trauma.**—Impalement upon a pitchfork (Colombat, 1), a fence picket or similar accidents, can cause severe and even fatal damage, mainly by opening up the peritoneum and adjacent cavities (bladder, etc.).

Rupture of the vaginal wall due to indirect violence producing prolapse of intestine through the posterior fornix is extremely rare. It has been caused by lifting a heavy weight and by a violent fall (Rommel, 2).

2. **Trauma During Coitus.**—Injuries during coitus are common and they are often of medico legal interest (Hoffmann, Sejournet, 3). They may be due to rape, undue violence or assumption of abnormal position during coitus, immaturity or senile involution. Neugebauer (4) has collected 150 cases. The fornix has been perforated; in one case the same man killed three wives by tearing the posterior fornix. Longitudinal vaginal tears and tears extending into the rectum are most frequent. Immediately violent hemorrhage may supervene; later infection and peritonitis can occur. Beumer (5) and Neugebauer (l. c.) report fatal cases.

3. **Labor.**—The most frequent and important cause of vaginal injuries is labor. Pressure and continued anemia of the parts, as seen in contracted pelvis, neglected labors and malpositions produce necrosis, sloughing and infection during the puerperium. If not fatal, fistulae, contractions and scars result. Tears may be circular, longitudinal, atypical, penetrating or submucous and are produced by many causes. Infantile vaginae (hypoplastic) and those of old primiparae are most vulnerable.

Circular tears are mainly in the upper third, in the vicinity of the cervix. If complete the injury is called kolporrhexis (5a) (tearing off of the vagina). Such tears regularly communicate with the peritoneal cavity and often extend far out into the parametria. They may be combined with rupture of the uterus. (Transverse presentations, forceps, the operator's hand, version.)

Longitudinal tears frequently are the continuation of cervical or perineal injuries. They may result from symphysiotomy or hebosteotomy, mal-

positions, disproportion, besides any of the causes mentioned above. The lateral sulci are regularly involved and the lower one-third of the vagina is oftenest affected. If deep, such tears extend into the paravaginal tissues, to the rami, or into the bladder or rectum.

Atypical injuries include avulsion of the urethra (Vogelsberger, 6), circular avulsion of part of the vagina (Esau, 7), plowing up of the vagina by projecting bones after craniotomy, etc. *Varices of the vagina* may be injured during labor. Profuse bleeding has led to rapid and fatal hemorrhage and has necessitated cesarean section (Riedinger, 7a). The mortality is high (over 60 per cent in 54 cases).

Submucous tears are frequent. Fibers of the levator ani, the triangular ligament and the transverse perineal muscles and the vesical fascia may be torn without injury to the mucosa of the vaginal tube. This condition, or more properly, the resulting defects which produce rectocele, cystocele, and prolapse, will be discussed later.

The various injuries mentioned may be followed by immediate and fatal hemorrhage, by acute peritonitis if penetration of the abdominal cavity has occurred, by paravaginal suppuration and by general infection and sepsis. Vesicovaginal and rectal fistulae, complete tears of the perineum, scars and stenoses are end results.

4. **Foreign Bodies** are introduced into the vagina for various and diverse purposes. Masturbation causes the introduction of such objects as hairpins, (Fabre, 8), bobbins, thimbles, stones, (Lahlich, 9). They are found in children and adults, often after having lain quiescent for years.

Perversion and brutality account for the bizarrest objects, not infrequently introduced with sufficient violence to produce immediate injury and symptoms. Catheters, hat pins, branches of wood, etc., are inserted for induction of abortion with resulting perforation of lateral or posterior fornices and consequent peritonitis or sepsis. Similar effects are produced by injection of fluids, including even strong caustics (Neugebauer (10)), which may occasion gangrene or air embolism.

Pessaries have been recovered after as long as 32 years' (Blondel, 11) sojourn in the vagina. Needless to say they are encrusted with salts, rough as a rasp, and firmly embedded in the vaginal walls, which have contracted below the foreign body. Ulceration into cervix, bladder, and rectum may result. In six cases collected by Neugebauer, carcinoma had developed from the irritation (Neugebauer, 12). The old wing pessary (Zwanck-Schilling) was the most frequent offender, but any pessary, including the best and most harmless, if unremoved and uncleaned, will eventually cause decubitus. Various ingenious contrivances to prevent conception (some vaginal, others cervical) have caused similar trouble, besides bringing about uterine and cervical infection (Ward, 12a). (Literature to 197 collected by Sharpe, 12b). *Vaginal Stones* due to urinary incrustation from vesicovaginal fistulae occur.

As a result of these and other injuries hematomata, fistulae and acquired stenoses develop.

5. **Hematoma** not due to pregnancy and labor is infrequent and usually small (Vallois, 13). Tense, livid, fluctuating tumors projecting

into or obliterating the vaginal lumen arise. If due to direct trauma, the wound of entry may be plugged by clot and the hematoma then develop. (See hematoma vulvae, p. 103.) During labor larger accumulations, usually continuous with vulvar hematoma, develop (Wimpfheimer, 14). (*See hematoma vulvae.*) Kaufmann (15) calls attention to the fact that rupture of a vaginal varix always causes hemorrhage into the vagina and not into the paravaginal tissues. He cites a case where air embolism occurred through the site of rupture.

6. **Fistulae** connecting either the urinary or intestinal tract with the vagina have been mentioned as possible end results of all the varieties of

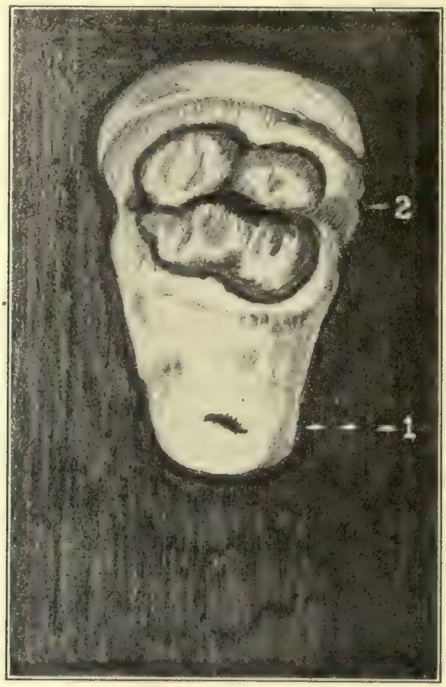

FIG. 106.—CERVICOVAGINAL FISTULA. Due to failure of dilatation of cervix during abortion, as seen through a speculum. (Case of Dr. J. Brettauer's.) 1. External os, (pin point) 2. False os on posterior surface of cervix close to fornix.

injuries just described. In addition they may be due to direct injury during an operation, or secondarily result postoperatively, from cutting off of the blood supply or decubitus from gauze or rubber tube drains. New growths, especially if treated too vigorously with radium, may break down and establish fistulae, which also may result from ulcerative processes such as esthiomène (p. 000).

Urinary Fistulae, Classification.—(a) Urethrovaginal, usually minute; (b) vesicovaginal of all sizes from complete absence of the bladder base and sphincter internus, with prolapse of the bladder fundus through the

hole, to minute tortuous tracts fixed to the pubic bone; (c) vesicocervicovaginal, usually small; (d) vesico-uterovaginal, the most uncommon form; (e) ureterovaginal, small, high in the lateral fornix.

Intestinal Fistulae, Classification.—(a) Fistulae of the small intestine result from prolapse of gut through a tear in Douglas cul-de-sac, with subsequent necrosis (attempt at criminal abortion), birth injury, operative injury in vaginal hysterectomy, etc.; (b) rectovaginal fistula in the great majority of cases is due to rupture of the rectovaginal septum in labor. The tears need not go through the sphincter. In complete tears after operative repair, a fistula may remain. Spontaneous healing of fistulae occasionally takes place. Absolute physiological rest and a contracted condition of the viscus (bladder) favors repair (Frank, 16).

The writer has seen a cervicovaginal fistula resulting from birth of the child into the vagina through a tear in the posterior lip of the cervix. For literature see Brünner (16a). The fistula remained after healing had taken place (Fig. 106) Brettauer (16b).

The temporary communications between dermoid cysts, hematoceles and similar cavities which have opened into the vagina will be referred to later (p. 454).

7. Acquired Stenosis and Atresia.—In this connection reference will be had to such changes as result directly from injuries due to labor, set up by foreign bodies and consecutive to the use of caustic employed to induce abortion (Neugebauer, 10). Puerperal gangrene may be followed by expulsion of the entire vaginal tube (Kümmel, Schutz, and Schrader, 17). Complete atresia with broad areas of agglutination, thin membranes, circular stenosis (often resulting from scars after forceps rotation) incomplete septa or mere folds may be the end result. The degree of secondary changes (hematocolpos, hematometra, etc.) will depend upon the completeness of the contraction or constriction. Complications such as septa and vesicovaginal fistula in combination (Brickner, 18) have been described (Fig. 107).

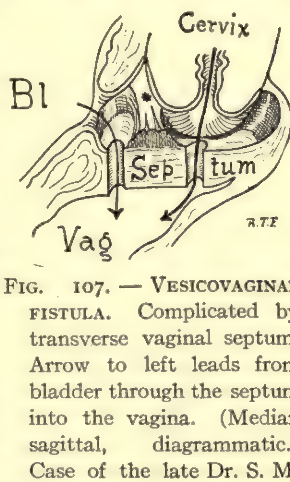

Fig. 107. — Vesicovaginal fistula. Complicated by transverse vaginal septum. Arrow to left leads from bladder through the septum into the vagina. (Median sagittal, diagrammatic.) Case of the late Dr. S. M. Brickner's.

II. INFLAMMATIONS

1. Flora of the Normal Vagina.—The normal vagina contains a definite bacterial flora as important to its health as the intestinal flora is necessary to the gut for proper performance of its function (19).

According to Loeser (20) a perfectly normal vagina contains (1) a large excess of the group of vaginal bacilli which coagulate milk and produce acid in the media. Among these is the Döderlein bacillus, bacillus vulgaris and bacillus ordinarius. (2) Pseudo-

diphtheria bacilli; (3) saccharomyces; (4) bacterium coli; (5) bacterium acidi lacti; (6) bacillus acidi lacti, comma variable, bacillus thetoides and various types of cocci, including staphylococci. Yeasts may be found.

In a perfectly healthy vagina only vaginal bacilli and comma variabile are found in the spread. As the vagina approaches the pathological, more and more of the other bacteria appear. When a yellow leucorrhea is examined, few, if any, of group one are seen.

The normal vagina gives an acid reaction. This is due to the lactic acid which results from fermentation of the glycogen stored in the vaginal epithelium. If the glycogen content is changed (reduced) by typhoid, Basedow, chlorosis, etc., the vaginal flora changes in consequence of the change in its substrat. The anaërobes and cocci increase at the expense of the normal flora and the vaginal epithelium permits a greater transudation of water—fluor albus develops.

Local diseases may also bring about a similar change. A sudden continuous inundation by other bacteria as seen in dysentery or cystitis may overwhelm the vaginal bacilli. Discharge from above (carcinoma cervicis, necrotic polypi, etc., gonorrheal endocervicitis) will exert a similar effect. For 8 to 10 days post partum the vaginal bacilli are crowded out by cocci. As soon as such overgrowth takes place the reaction of the vagina becomes less acid and may turn alkaline.

The vagina is like the skin; upon both in health grow all varieties of bacteria. If given a point of entry, by breaks in continuity or by maceration, virulent germs may produce inflammation.

The streptococcus requires a wound, the gonococcus maceration (Veit, 21). Such bactericidal action as is found in the vagina is due to lack of oxygen, to leucocytes and to bactericidal tissue juices, not to the lactic acid present (Menge, 22).

In the main the subject of vaginal flora is one for the bacteriologist. The sterility of the infant vagina has been studied by Schmidgall (22a); one day after birth, bacteria are found. The pioneer work on the flora of the vagina in pregnancy has been performed by Döderlein (19), Krönig (22b) and Menge (22). The bacteriology will be further considered under puerperal infection.

2. **Vaginitis.**—Vaginitis is an inflammation due to the bacterial infection. The process may be acute or chronic. Depending upon its severity, vaginitis is classified into catarrhal, membranous or gangrenous.

Catarrhal Vaginitis.—Catarrhal vaginitis may be diffuse or circumscribed (colpitis granulosa). The process consists essentially of subepithelial round-celled infiltration, in which the round cells may aggregate at the tip of papillae and cause disappearance of the overlying epithelium. When this desquamation occurs, small, red, easily bleeding areas are found scattered over the mucous membrane. These spots are readily seen and felt (as nodules of infiltration) in the circumscribed form (c. granulosa). They are lost in the general redness and swelling of the diffuse variety, which microscopically shows as a widespread congestion and dilatation of vessels accompanied by an increase in lymphocytes, between the discrete foci. Grossly, swelling, redness and discharge with increased desquamation are prominent. Almost invariably an endocervicitis and often a vulvitis accompanies the vaginal inflammation.

Etiologic Factors.—Acute.—Gonorrhea is frequent in children; according to Frankel (23), 80 per cent of all vulvovaginal infections. The gonococcus has also, but rarely been demonstrated upon, in or below the epithelium in adults (Bumm, 24), because the adult vagina is resistant to this germ. Likewise it has been found in the vagina after complete hysterectomy after which the question of macerating cervical discharge can no longer enter as the sole factor (Döderlein, 25). Doubtless, however, the vaginal mucosa is more atrophic and less resistant after castration, just as it is after the climacterium. In adults no chronic gonorrheal vaginitis occurs. The vagina rids itself of the invasion after a short acute stage.

Infection may be carried from the anus, especially in diarrheas, from the bladder in cystitis. Irritating and infected discharge from breaking down uterine cancer, sloughing fibroids, vesicovaginal and rectovaginal fistulae, encrusted pessaries and other foreign bodies, are all conducive to acute or chronic vaginitis.

Etiologic Factors—Chronic.—As the process becomes more chronic the circumscribed types are more in evidence; discrete nodules (colpitis granulosa) (Schirschoff, 26), erosions if the epithelium has desquamated (colpitis erosiva), pigmented spots remaining as the nodules are absorbed or erosions heal (colpitis maculosa), papillomatous projections from irritation of the papillary body (colpitis papillomatosa), one or all may result from the inflammation.

An almost physiological process, but always accompanied by some inflammation, is *senile vaginitis* (colpitis vetularum), in which the atrophic epithelium is eroded, and adhesions obliterating the fornices, hiding the cervix and producing senechiae develop.

Colpitis emphysematosa occurs most often in pregnancy (Eisenlohr, 27). Multiple small, tense cysts from pin-head to pea size, are found beneath the epithelium of the vagina, and of the vaginal portion of the cervix. When opened, gas trimethylamin—(Zweifel, 28) instead of fluid, escapes. Examination shows gaps in the connective tissue and lymph spaces (Waldstein, 29) with many bacteria—of the coli group (Lindenthal, 30). As the gas formation distends the cysts, the bacteria appear to be fewer in number. Some of the cysts may have an endothelial lining; round-cell infiltration, and occasional giant cells may be found. The disease is harmless and is self-limited, disappearing within a few weeks to four months postpartum.

Thrush (Soor) due to various fungi (Herff, 31) either causes or appears in mild, superficial inflammations. The fungus does not penetrate below the desquamating layers of epithelium. The disease is noted in pregnancy and in diabetes. It may cover large areas and must be differentiated from the serious membranous vaginitis.

Castellani (Journal of Tropical Med. & Hyg., 1916, April) reports monilia pinoyi, a hyphomycete as cause of vaginitis in a pregnant woman.

Membranaceous vaginitis (exfoliative vaginitis) is a rare condition resembling membranaceous enteritis and dysmenorrhea membranacea. Superficial molds of the vagina are repeatedly cast off (Gellhorn, Kerwin, 26a). The deeper and more virulent processes are divided into superficial

exudative (croupous) and necrotic (diphtheritic) varieties. In the former the grayish or yellowish exudate can be pulled off readily; in the latter, if removed, deeper defects of the mucosa become visible. True diphtheria (Klebs-Loeffler bacillus) is classified under the necrotic form. In severe cases the process ends as a gangrenous vaginitis, which, if deep, becomes a paravaginal infection causing *phlegmonous* vaginitis (v. Lingen, 40).

Etiologically the same cause may produce either mild or severe types of inflammation, depending upon the virulence of the bacteria, the resistance of the affected individual, and upon the local conditions (for instance, a big, complicated, poorly draining vaginal and parametrial tear, a debilitated child with diphtheria, etc.).

Infectious diseases, such as scarlet fever, measles, smallpox, often show a complicating vaginitis. Probably vaginal efflorescences break down. Veit considers these diseases prolific causes of atresias and stenoses existing since childhood. In typhoid (Keen, 32), dysentery (Eppinger, 33), pneumonia (Brose, 34), diphtheria (Kaufmann, Goodmann, 35), cholera, vaginitis varying from the mild exudative to the phlegmonous is on record. During the course of the severe systemic disease the vaginitis is rarely noted, unless a foul discharge, or necrotic pieces of tissue attract attention. More often the condition is first recognized at autopsy, or after recovery, when disability becomes evident (Keen, l. c. 32).

Puerperal vaginal infections show all degrees of severity. Highly virulent hemolytic streptococci may gain entrance through a small lesion and produce fatal bacteremia without noticeable local changes. The local condition may predominate in the form of extensive superficial exudation on the wounds, in which case the protective granulation wall composed of leucocytes may interpose an effective barrier. Extension into the uterus by way of the surface of the mucosa, progression through the paravaginal lymphatics, or by means of a thrombophlebitic process or a diffuse gangrenous vaginitis may result. Finally, any or all of these forms may occur in combination. (See puerperal infection, p. 480).

Uremic ulcers described by Eichhorst (36), noted in severe cases of uremia, fall into this group of vaginal infections.

The ulcus rotundum (Zahn, 37) which appears as a single or multiple punched-out area, with musculature or paravaginal tissue as base, may be partly on an arteriosclerotic basis (ischemic, Beutner (38), Beckman, 39); but infection later unquestionably enters into the process.

Decubital ulcers common in prolapse of the uterus and its accompanying recto- and cystocele, must be ascribed to drying of the vagina, trauma with consequent excoriation, and finally infection.

Discharges from ulcerating and necrotic cervical or uterine carcinomata, from sloughing fibroids, from rectovaginal or vesicovaginal fistulae may eventually produce membraneous vaginitis as well as catarrhal changes. The discharge macerates the epithelium, helps pathogenic bacteria to overgrow the normal vaginal inhabitants, and ends in membranes, ulcers, or gangrene.

Decubitus by pessaries, drainage tubes, gauze, etc., have been mentioned (p. 137).

Phlegmenous vaginitis (paravaginitis) is probably a disease of the connective tissue. Occurring most commonly after typhoid (v. Lingen, 40), it produces a gangrene of part or all of the vaginal tube, a line of demarcation eventually develops and the slough is cast off (Kretschmar, 40a).

Atresia or stenosis may result. Less diffuse paravaginal infections result in the puerperium, after operation, etc. (Veit, 3: 257); considering the severity of the process, peritonitis or a fatal outcome are rare.

Caustic necroses and poisoning by absorption hold an intermediate position between injuries and inflammations. Caustic action of a superficial nature may result from ichthyol or aristol. Deeper and more destructive lesions (Busse, 41) are produced by iron chloride, zinc chloride, carbolic acid, etc., used for therapeutic or abortifacient reasons.

Poisoning by absorption from bichloride of mercury douches have been repeatedly recorded (Peterson and Haines, 42). Kaufmann (43) reports a case after hysterectomy, so that we know that the absorptive surface was surely limited to the vagina. In bichloride poisoning by mouth a severe vaginal inflammation, resembling mercurial stomatitis may be set up. Heberda (44) records a case of arsenical poisoning.

III. SEQUELAE OF VAGINITIS

A. **Atresia and Stenosis** of the vagina. Passing reference has been made to these conditions as sequence to gross injuries (p. 138). Much more frequently no antecedent etiological factor, no history of injury or inflammation can be elicited. Until 1896 when Nagel (45) raised the question, almost all such cases were regarded as congenital. Since then he, Veit (46), and R. Meyer (47) have gone to the opposite extreme and now consider every case that occurs without duplication of the genital tract, and with well-developed uterus and tubes as acquired and due to infection. Stratz, Kermauner (48) and others believe that congenital atresia can occur with well-developed and single genitals. The question is fully threshed out by v. Rosthorn (49).

Atresia.—*Agglutination of the labia* was described under vulva (p. 105). The hymen may be imperforate at birth (Chrobak, 49) in which case no doubt as to the congenital origin of the closure can be entertained, but the closure may be due to vaginitis in utero as well as to a failure of development (Vitrac, 50).

Retrohymenal membranes have been described (Bell, 49). In Bulius' (51) case, that of a newborn, a scar traversed the membrane, bespeaking intra-uterine vaginitis and agglutination. Such cases are noticed at or shortly after birth because of the bulging which appears when the infant cries.

When symptoms from atresia arise at puberty, it is difficult from the objective findings to determine the cause and time of origin of the closure. Veit denies that a congenital closure could have existed without being noticed or without producing symptoms in childhood. Such positiveness is not justified. The majority of cases are doubtless due to vaginitis during childhood. Broad areas of adhesion are always of inflammatory origin. The resulting hematocolpos, hematometra and hematosalpinx are discussed further on (p. 498).

B. **Stenosis of the Vagina.**—This condition occurs most commonly at the junction of the upper and middle third, or junction of lower and middle third. The stenosis appears as a thick, fleshy membrane, which, except for a small opening, impresses as a complete roof or top of a blindly ending sac. Multiple superimposed septa are recorded (Thompson, 52). The reddened and granular cervix may be attached to the membrane at some part of its periphery.

Ostermann's (53) criteria of congenital origin of such septa (situation in upper third of vagina, absence of scar tissue, homogeneousness and softness of membrane) are not convincing. Occasionally their development, post partum, has been watched (Odebrecht, 54). In others the history of antecedent infection will be decisive.

From what has preceded it will be clear that the majority of atresias and stenoses, when no duplication of the genital tract is found, are due to injuries or inflammations occurring in post-natal life. Of the remainder, in which an antenatal origin can be shown, a majority will again be due to agglutination of opposing surfaces. Only a small minority may fall into the class of developmental deficiencies.

The literature to 1895 has been gathered by the indefatigable Neugebauer (55). In 15,000 of his cases six atresias were found. From the literature he gathered 33 puerperal, 6 hymenial (congenital), and 12 due to defective vaginal anlage.

IV. SPECIFIC INFLAMMATIONS

Tuberculosis of the Vagina.—Tuberculosis of the Vagina is more frequent that that of the vulva, according to Williams (56), though among the rare conditions. It is practically always secondary to tuberculosis elsewhere—uterus (Kaufmann, 57), tubes, peritoneum, lungs (Springer, 58), bladder (Jones, 59), rectum (Kaufmann, 57). The case described by Friedlander (60) may have been primary. Most often the lesions are near the cervix or close to the vulvar entrance.

The commonest form is the typical tubercular ulcer, serpiginous in type, with tubercles at its edges; next in frequency is the papillary variety and most uncommon are diffuse, non-ulcerating tubercles. Vesicovaginal (Catuffe, 61) or rectovaginal (Jones, l. c. 59) fistulae may develop, either before or secondary to the vaginal lesion, the perineum, vagina and entire

genital tract may be involved (Emanuel, 62), or a vulvar and vaginal lesion coexist (Zweigbaum, 63).

The commonest source of infection is from contiguous lesions (uterus, cervix, vulva, etc.); hematogenous infection is rare. Coital infection cannot be denied, but has not been proven. The histological details are characteristic of tuberculosis everywhere, giant cells, epitheloid tubercles, tubercle bacilli in spreads, sections and culture. Carcinoma or syphilis, which alone come into question, can be differentiated readily.

Syphilis of the Vagina is of rare occurrence and of minor interest. Primary and secondary lesions at the vulvovaginal junction may extend into the vagina. Rarely lesions of the cervix extend into the fornix. For the scant literature see Neumann, Winter, Oppenheim (63a).

Gummatous vaginitis (perivaginitis gummosa—Birch-Hirschfeld, Lehrbuch, 1887, 2, p. 794) by converting the vagina into an inelastic tube, may cause dystocia.

V. VAGINAL CYSTS

Vaginal cysts are of fairly frequent occurrence. They are usually accidental finds unless their size, protrusion from the vagina or hindrance to coitus causes them to be noticed. The cysts are commonly unilocular, of small size (pea to walnut), but some have reached the dimensions of a child's head. They occur in the anterior or lateral vaginal walls, rarely in the posterior. The small cysts usually protrude into the lumen of the vagina, so that they are often merely subepithelial and consequently shine through as thin-walled, bluish projections. Large cysts develop outward into the ischiorectal fossa or spread into the base of the broad ligament and may displace the uterus. Rosarylike strings of cysts are frequently noted, and in one case (Bonny and Bryden Glendining, 64), a widely distributed crop of small cysts appeared scattered over the vaginal mucosa, apparently secreting (?) six ounces of mucus daily.

The cyst wall is composed of connective tissue, not uncommonly surrounded by a layer of unstriped musculature, and has a very varied epithelium. The epithelium may be low cuboidal (Fig. 108), high cylindrical ciliated (Wanner, 65), or squamous; often high stratified. It may be lacking in areas and cysts without discoverable epithelial lining are not uncommon (Piqué, 66). Great variations within the same cyst are encountered (Fig. 109). The inner lining may form folds or even papillary projections (Falkner, 67).

The cyst content, especially in the smaller cysts, is glairy mucus which may be blood-tinged red to brown. The larger cysts often have cloudy yellow to brown fluid with a thick claylike consistence. Cholesterin crystals or even more rarely, concretions (Gellhorn, 68) may be constituents.

The etiology of the cysts is mainly of theoretical interest. For the

smaller cysts, especially if multiple, vaginal glands (v. Preusschen, 69), aberrant vestibular or cervical glands (cylindrical epithelium, l. c. 64) and also derivation from Gärtner's duct—wolffian duct (Veit, 70) come into question. The larger cysts, if lateral to the vagina and extending

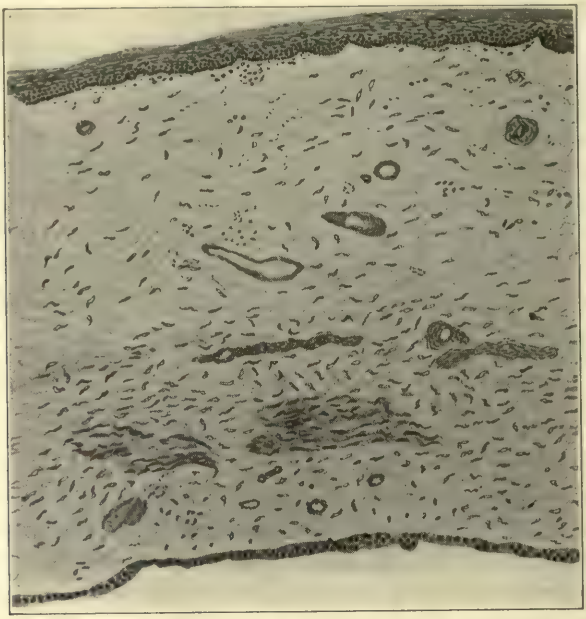

FIG. 108.—VAGINAL CYST. (L.P.) Upper limit shows stratified squamous vaginal epithelium with low papillae. The middle portion is occupied by the vaginal wall. Below is low cuboidal epithelium lining the cyst wall.

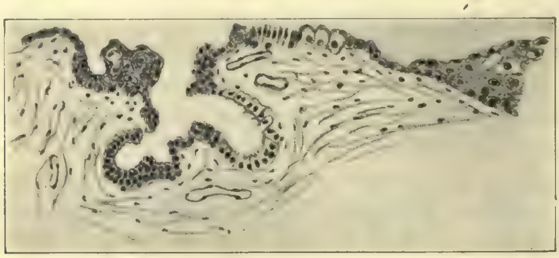

FIG. 109.—PART OF LINING OF A VAGINAL CYST (GÄRTNER'S DUCT DERIVATION). (M. P.) The epithelium from left to right shows low cuboidal, stratified squamous, transitional, ciliated (on right side of depression), columnar, goblet and again squamous characters.

along the cervix into the broad ligament, are surely of wolffian derivation. Such cysts are in the vaginal wall (R. Meyer, 71). Genetically they are similar to parovarian cysts.

Epidermoid implantation cysts consequent to displacement of small epidermal islands by trauma, labor or operation are frequent but unimportant (Buerger, 72). They are lined with squamous epithelium and

their content is turbid, desquamated epithelium. Quinby (72a) describes a larger epidermoid cyst of the vesicovaginal septum, which caused vesical bleeding; Curtis (72b) a dermoid, size of an orange, lateral to the cervix (contents, sebum and hair).

Freund (73) has mentioned Müller's duct, in ununited double vagina with the atrophic side running in the wall of the well-developed one, as a possible cause of vaginal cysts. Accessory, cystically dilated ureters may simulate cysts (Conitzer, 74). Ecchinococcus cysts in the pelvis may appear in the vaginal region (Freund, 75).

Cysts in the urethrovaginal septum may be true vaginal cysts (Neel, 76).

FIG. 110.—MULTIPLE VAGINAL CYSTS COMPLICATING PREGNANCY. The largest cyst (size of coconut) could be forced outward so as to present in the buttock as shown in the photograph. The topmost cyst reached into the base of the broad ligament.

Vaginal cysts have been observed in the newborn (Vassmer, 77).

Guder (78) records 23 cases observed during labor; in seven the tumor was drained during labor to overcome dystocia.

The writer has reported a case of large multiple vaginal cysts necessitating cesarean section because the enormous vaginal varicosities present prohibited incision and drainage from below (Frank, 79) (Fig. 110). Falkner described malignant changes in a vaginal cyst (67). Recent literature is contained in Cullen (80). Stokes (81) has collected the literature to 1899.

VI. BENIGN TUMORS OF THE VAGINA

Fibroepithelioma, Papilloma, Condyloma.—Kiesselbach (82) described multiple papillomata. Condylomata are not infrequent in pregnancy. The writer has seen a large collection on the cervix and in the posterior fornix in a patient who was gravid and had gonorrhea. The condylomata are pinker, softer, and unindurated in contrast to carcinoma.

Plexiform neuroma was described by Schmauch (83). It is the only case on record.

Rhabdomyoma was seen by Bidone (84). The question arises whether this was not a malignant tumor or a teratoma.

Fibroma, Fibromyoma, Adenomyoma.—Smith (85) in 1902 collected 100 cases and Patel (86) the next year gathered 160 cases. Müller (86a) in 1914 reports 112 cases. The condition is not frequent. The tumors may occur in any part of the canal, appearing either as sessile or polypoid growths. They form a hard, usually smooth mass projecting into the lumen, may protrude from the vulva and then readily ulcerate. In one case a serious hemorrhage developed from the tumor (Littauer, 87). The majority of these growths are well encapsulated.

The tumors are in the large majority fibromyomata, similar in morphology to uterine ones. Like these, they undergo hyaline degeneration, become edematous or can slough. Pure fibroma is uncommon (Hasenbalg, 88). Adenomyoma (Moraller, Amann, 89) containing glands with and without cytogenic stroma, have been described. Etiologically, vaginal glands, wolffian duct and adenomyositis (for those in the posterior fornix, see Uterus, page 212) come into question.

Guder (l. c. 78) collected 18 cases complicating pregnancy, in which cesarean section was performed three times, five times the tumors were enucleated either during or before labor.

Hofmokl (90) described a case in which the tumor arising from the vaginal wall, reached the size of a child's head. Whether a tumor whose pedicle arose from the parametrium (Merkel, 91), or those situated in the vesicovaginal septum (Broun, 92), properly should be classified with vaginal tumors, I will leave an open question.

Kehrer (Monatsch. f. Gynäk. 1909. 30:731) gives the most recent review of the literature.

Granuloma of the Fornix resulting from fallopian tubes adherent in this situation after vaginal hysterectomy, cause readily bleeding small tumors, which disquiet because of their resemblance to metastases. The writer has personally seen two cases, one after hysterectomy for corpus carcinoma, the other for chorioepithelioma. Under very low magnification the mass resembles a papilloma (Fig. 111). Higher power shows the structure of normal or inflamed tubal folds, which, if the condition in question is not considered, may be mistaken for adenoma or adenocarcinoma (Fig. 112).

FIG. 111.—PROLAPSED FALLOPIAN TUBE ADHERENT TO VAGINAL FORNIX. (Very low power.) After vaginal hysterectomy for chorionepithelioma of uterus.

FIG. 112.—MEDIUM POWER OF SMALL, MARKED PART OF FIG. 111. Shows tubal folds cut in various directions. Note regularity of epithelium, absence of invasive tendencies.

VII. MALIGNANT TUMORS

1. **Carcinoma of the Vagina.**—Carcinoma of the vagina is infrequent. Primary cancer is very rare (Williams, Schottländer, 93), secondary cancer due to extension of contiguous growths from the cervix (Eppinger, 94), metastasis from uterus, ovaries, etc., less so. Schlund (95) collected 273 primary cases in 1913.

1. *Primary.*—The age incidence is from 30 to 40 years, though Falk (96) reports a case at 19 years, Ward (96a) at 20 years, and v. Winckel (97) saw some between 20 and 30. It is rare in nulliparae (Veit).

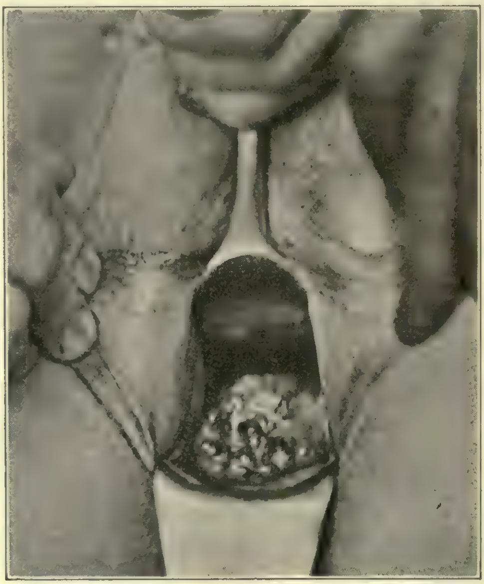

FIG. 113.—CARCINOMA OF MIDDLE THIRD OF VAGINA. Posterior wall. Inoperable because of extensive involvement of paravaginal tissues.

The most frequent situation is in the posterior fornix, nearly two-thirds being found there (Döderlein and Krönig, 98), next is the lower third of the vagina, the middle portion being less often involved.

The growth is rarely noticed in its early stages. Ewing says that the initial growth appears as a wart, as a superficial nodule or a diffuse infiltration (v. Winckel, 97). Later on the chief types are, (1) a circumscribed projecting tumor with infiltrated base, its surface nodular or papillary and showing early ulceration. The ulcer is craterlike, with dirty nodular base and indurated edges (Fig. 113). (2) Diffuse infiltrating type which extends rapidly, converting the vagina into an inelastic tube with nodules and masses projecting into its lumen.

Fornix cancer extends upward rapidly, producing early involvement of the cervix. Consequently, except in very early cases, it is difficult to decide whether the growth originated from the cervix or vagina (Döderlein and Krönig, 98). Paravaginal exten-

sion is also early because the weak and thin vaginal tube can offer but little resistance. Fixation of the growth is therefore an early sign. The rectum is involved more often and more frequently than the bladder, not only because the situation of the growth is oftener on the posterior wall (1 : 3) but also because the main lymph channels run toward the rectum and empty into the superior hemorrhoidal and mesorectal glands. The same pelvic glands that drain the cervix are also implicated. The lower third of the vagina infects the inguinal glands. Extension to the vulva is late and not frequent, and vulvo-vaginal growths have not often been reported. As the disease progresses, rectovaginal and vesicovaginal fistulae may develop. Cachexia takes place early, and the course is short, Williams (l. c. 93) placing the shortest at 8 months and the longest at 26 months, and the average at 16½ months. The operative prognosis is most unfavorable, as even after radical combined perineo-abdominal removal early, local recurrence is the rule. A few permanent cures are reported (Legueu, 100). Metastases occur in the internal organs with about the frequency seen in carcinoma of the vulva, but are infrequent compared to local recurrences.

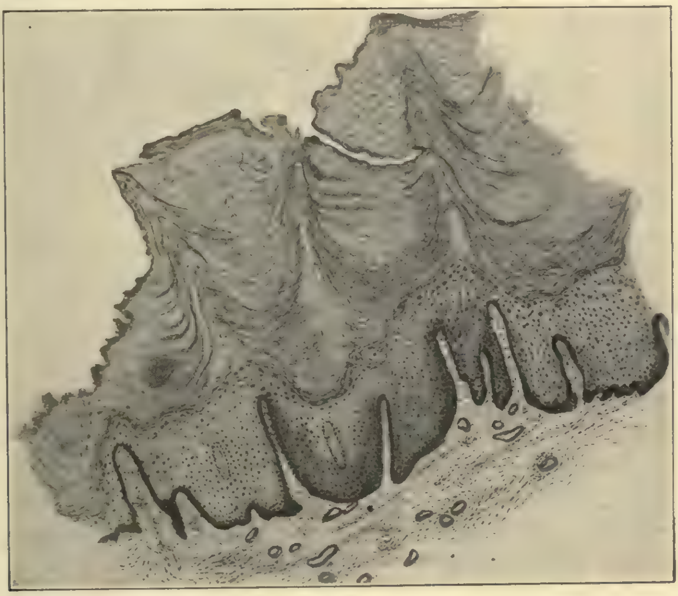

FIG. 114.—LEUKOPLAKIA OF VAGINA. (M.P.) Below is the normal connective tissue of the vaginal wall. The papillae are high and narrow. The epithelium is much thickened and the cornified layers on top are enormously increased. Toward the left the epithelium is less hypertrophied.

Etiologically, irritation from continued wearing of a pessary (Maly, Schlund, 101) or from a prolapsed vagina exposed to trauma (Schlund, Fleck, Schmidt, 102) has been observed but is comparatively infrequent. Leukoplakia as a forerunner has been noted repeatedly (v. Franqué, 103). (Fig. 114.) See Leukoplakia of vulva, p. 113. It appears to the writer that the mechanical friction exerted by the cervix may account for the favorite location of primary vaginal cancer in the posterior fornix, although why the anterior fornix remains regularly unaffected is not quite clear except that macerating discharges do not collect as much anteriorly.

Histogenetically, vaginal glands, vaginal cysts, and Gärtner's duct, come into question in connection with adenocarcinoma (Hirsch, 104), which is less frequent than squamous cell cancer. The carcinoma may show alveoli with mucous glands, resemble adenoma malignum (Argand and Piollet, 105), or give mere indications of an adenomatous type (Fig. 115).

The squamous cell variety is of the type of carcinoma simplex. Less often epithelioma with cornification and pearl formation (Taylor, 106) is found. Types classed as endothelioma have been reported. They impress more as carcinoma developing in endothelial spaces (Jellet, 106a).

2. *Secondary.*—Extension of cervical cancer to the vagina is the rule (Schottländer, 107). When a growth of the portio extends directly to the vagina, the connection is self-evident. When an as yet unnoticed,

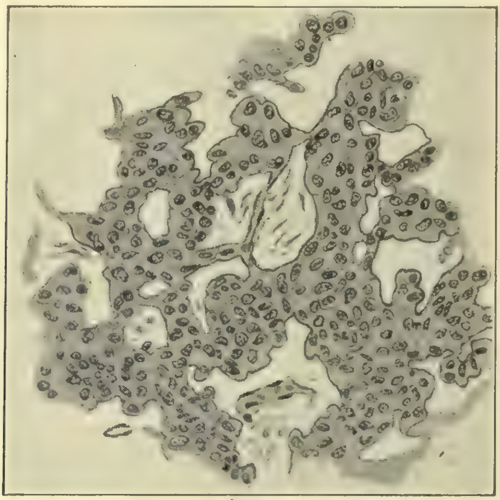

FIG. 115.—CARCINOMA OF VAGINA. Assuming the characters of adenocarcinoma. The main mass of the tumor is of squamous type.

intracervical or corporeal neoplasm extends by way of the parametrium or by retrograde processes through lymph or blood channels (Milner (108), Cullen, 108) to the vagina, a primary occurrence may be simulated. Metastases from the uterine body (Hellendal, 108a) or ovary (Semmelink, 109) are not common. Implantation occurring during vaginal hysterectomy has been mentioned in connection with vulvar cancer (p. 123) and likewise occurs in the vagina (Leisewitz, 110). Cancer of the rectum (Lauenstein, 111) or bladder may involve the vagina.

The morphology of metastatic carcinoma is not distinctive except that usually a typical adenoma malignum indicates a primary focus in the corpus uteri.

Vaginal adenoma (Winter) will be discussed under cervix as adenomyoma of the fornix (see p. 212).

Grad (Am. Jour. of Obst. 1918, 77:588), reports spontaneous perforation of the vaginal vault behind the cervix by a papilliferous cystadenoma of the ovary which also studded the peritoneum. The cauliflowerlike mass filled the upper vagina. The condition was still operable.

Differentially, sloughing benign tumors may closely simulate a carcinoma. The microscope must decide. If the carcinomatous process causes a stenosis of the vagina below the growth, the resulting retention of pus and discharge and the hidden situation of the cancer may occasion some doubt. The indurated ulcers due to long-retained pessaries superficially resemble cancer, but rapidly heal upon removal of the cause of irritation. In one instance in the writer's experience, a punched out, slightly indurated ulcer of the posterior fornix occasioned doubt. It was not specific, malignant or otherwise characteristic. (Cultures, animal inoculation.) Possibly it corresponded to the ulcus rotundum of Zahn (p. 142). Here the diagnosis was made by the absence of positive criteria.

2. **Sarcoma of the Vagina** (exclusive of sarcoma botryoides).

These tumors belong to the uncommon forms. McFarland (112) in 1911 collected 68 cases exclusive of the mixed tumors of children (sarcoma botryoides). (See also Bland, 113.)

The tumors appear as nodular, sessile, polypoid or more rarely as diffuse stenosing growths (Jellet and Earl, Seitz, 114) in any part of the vagina. At first the vaginal epithelium covers them, later necrosis occurs and penetration of the neighborhood takes place. Huge necrotic, hemorrhagic and cystically degenerating masses may result. Metastases are not uncommon, but appear late (Bland, l. c. 113), gland involvement is rare. Permanent cure has been infrequent (Spiegelberg, 115).

Histologically, myxomatous, round-celled, polymorph and giant cell, (v. Rosthorn, 116), spindle, alveolar, perithelial (Klien, 117) and telangiectatic (Kaufmann, 118) varieties have been reported.

A few melano sarcomata are on record (Boldt, Graefe, 119). In these the course can be hyperacute as in Graefe's case where death took place 15 days after the second operation for recurrences (4 weeks after first operation).

Metastatic vaginal sarcoma (Hofmokl, 120) can occur from uterine primary growths (Kaufmann, l. c. 15, 2: 1022) especially in the urethral region.

The diagnosis early in the course of the disease can be made only by the microscope, as nodular or polypoid fibromyomata will give the same symptoms and appearance. Later after necrosis has begun, sloughing fibroid or cancer will require differentiation.

Of the 68 cases collected by McFarland 58 were in adults and 10 in infants. The anterior and posterior walls were most frequently affected, vulvovaginal and circular growths being uncommon.

3. **Mixed Tumors of the Vagina (Sarcoma botryoides) in Children.**

These tumors, which have regularly been classed with sarcomata, are,

as Wilms (121) has shown, true mixed tumors or teratomas with development of the mesodermal constituents alone. McFarland (112) has collected 33 cases, Veit (122) places the number on record as 40.

They are noted rarely at birth, usually develop in early infancy, and in a few cases have not shown signs of malignancy until after puberty (Ahlfeld, 123).

The appearance of a polyp at the vulva in infancy has been the usual mode of onset. This growth regularly attaches to the anterior vaginal wall and promptly recurs after removal. The increasing number of red or pink pedunculated masses distend the vagina, sessile growths infiltrate its walls and break early into the bladder. Necrosis of the covering epithelium is followed by suppuration, which produces pyometra and purulent peritonitis. Death may also result from blocking of the ureters and pyonephrosis. Metastases may appear in the lungs and other organs, rarely in the inguinal or pelvic glands. The regular mode of advance is by extension, which includes also the vulva and parametria, but very rarely the rectum (D'Arcy Power, 124).

The course commonly is short. In Demme's (125) case, a small tumor was noticed at birth, but showed no signs of malignancy until the fifth year. Only one permanent cure is recorded (Volkman-Schuchardt, 126), in which a recurrence was removed after 6½ months, 10 years later the child was still well. All other cases have recurred at once.

The histology of these tumors is varied. The one trait they have in common is an origin from mesodermal tissue of the early embryonal period. A few are simple polypoid sarcomata, the majority, in the main, are spindle-cell sarcomata but show other mesodermal derivatives (Wilms). The most regular component is myxomatous tissue (Soltmann, 127). Striped muscle fiber is a frequent (Kolisko, 128), but not a necessary constituent (Pick, 129). Unstriped muscle, giant cells, round cells, cartilage (Pernici, 130), and even epithelial cell groups (Hauser, 131) are reported. Metastases into the skin (Kalustow, 132), peritoneum (Koerner, 133), ovary (Demme, 125), lung (Hurdon, 134) are infrequent. The metastases may contain the same mixed constituents as the primary growth (striped muscle in the lung, Hurdon), or prove simple spindle or round cell aggregations.

Any polyp coming from within the vagina of an infant must be regarded with utmost concern and requires expert microscopical examination. The prognosis is so poor that few operators would consider the radical colpo-hysterectomy by the sacral route, practiced by Israel (135) on a nine months old infant; recurrence in three months.

Chorionepithelioma has occurred ectopically in the vagina. It will be discussed in the chapter dealing with the pathology of pregnancy (p. 471).

Hypernephroma metastases have been reported in the vagina appearing there before the primary kidney tumor was recognized (Gellhorn, 136). This author has collected nine other cases from the literature.

VIII. VAGINAL PARASITES

Vaginal parasites are not of much importance. Parasites escaping from the anus may enter the vagina, especially in neglected infants—oxyuris vermicularis (136a)—producing superficial irritation. Trichimonas vaginalis may produce vaginitis (De Lee, 137), although found present in 30 to 40 per cent of all vaginal secretions carefully examined (137a) whether vaginitis existed or not. Amoeba urogenitals has been described. In Egypt, vaginal papillomata and leathery infiltration of the vaginal wall as a result of Bilharzia (Schisostomum hematobium), is very common (Horwood, Milton, 138). Rhabditis pellio (139) and anguillulo aceti (vinegar eel) (140) are rare findings of little importance. Ecchinococcus cysts are never primary in the vagina. Secondarily, they may approach the vaginal walls as they grow in the pelvic connective tissue (see p. 443).

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24. BUMM. Veit's Handbuch. 2: 54.
25. DÖDERLEIN, A. Monatschr. f. Geburtsh. u. Gynäk. 5:34.
26. SCHIRSCHOFF, D. Zeitschft. f. Heilk. 1900. 227.
26a. GELLHORN, G. Am. Journ. Obst. 1901. 44: No. 3.
KERWIN, W. Exfoliative vaginitis. Surg., Gynec. & Obst. 1918. 27: 151. (In one year 40 epithelial casts of vagina were passed at 1 to 3 weeks interval.)
27. EISENLOHR. Ziegl. Beitr. 1888. 3: 101.
28. ZWEIFEL. Arch. f. Gynäk. 1887. 31: 363.
29. WALDSTEIN. Zentralbl. f. Gynäk. 1912. 36: 650. (Berichte.) (Histology, Lymphspaces clothed with endothelium resembling giant cells.)
30. LINDENTHAL, O. Wien. Klin. Wochenschft. 1897. Nos. 1 and 2.
31. v. HERFF. Ueber Scheidenmykosen. Sam. klin. Vorträg. N. F. No. 137. (15 monilia albicans, 3 monilia candida, 1 leptothrix, 1 yeast.)
32. KEEN, W. W. Urination and menstruation per rectum. Ann. of Surg. 1919. 69: 606. (Due to slough after typhoid.)
33. EPPINGER. Zeitschft. f. Heilk. 1881. 1.
34. BROSE. Zeitschft. f. Geburtsh. u. Gynäk. 24. (Expulsion of gangrenous vaginal mucosa five days after crisis of pneumonia.)
TORRVELLA, M. A. Revista Med. Mexico. 1919. 1: 245. Abst. Jour. Am. Med. Assoc. 1919. Sept. 20. p. 946. (Pure culture pneumococcus in virgo with colpitis.)
35. KAUFMANN, E. Lehrbuch der Spez. Anat. u. Path. 1911. 2: 1039. (Describes fatal case in child of 1½ years where the throat diphtheria had healed, but a noma-like genital gangrene developed.) (Lit.)
GOODMAN, A. L. Am. Jour. of Obst. 1914. 272.
36. EICHHORST, H. Med. Klin. 1912. No. 38. (Similar ulcers as are found on gut, mouth, larynx, and skin in uremia.)
37. ZAHN. Virch. Arch. 95: 67 and 388.
38. BEUTTNER. Monatschft. f. Geburtsch. u. Gynäk. 3: 121.
VEIT. l. c. 3, i; 180. (Observed two cases of ulcus rotundum which he ascribes to an infection similar to ulcus molle; does not mention occurrences of bubo.)
39. BECKMAN. Ann. de Gynéc. 1897. May.
40. LINGEN. Arch. f. Gynäk. 59. No. 3. Or Ann. de Gynéc. 53. Feb. (Five due to typhoid; 1, pneumonia; 1, bronchitis; 8, cause unknown.)
40a. KRETSCHMAR. Ueber spontane Scheidengangrän (Paravaginitis phlegmenosa dissecans). Mittelrh. Ges. f. Geburtsh u. Gynäk. 1910. Nov. 13. Ref. Monatschft. f. Gynäk. 1911. 33: 393.

(Thirty-three years after menopause, chill, 9 days later cast of vagina and portio expelled including superficial muscle layer.)

41. Busse. Arch. f. Gynäk. 56: 489. (Due to iron chlorid.)
42. Peterson and Haines. A Textbook of Legal Medicine & Toxicology. W. B. Saunders & Co. 1904. 2:391. (Of 231 cases of bichloride of mercury poisoning, collected since 1879, 141 were due to irrigations of vagina, and uterus; of these 48 were fatal.)
43. Kaufman. l. c. (35). 2: p. 1038.
44. Haberda. Wien. Klin. Wochenschft. 1897. No. 9.
45. Nagel. Zeitschft. f. Geburtsh. u. Gynäk. 1896. 34.
46. Veit, J. Berlin. Klin. Wochenschft. 1896. No. 16.
47. Meyer, R. Zeitschft. f. Geburtsh. u. Gynäk. 1896, 34. 1897, 36. (Etiology Atresia.)
48. Stratz. Zeitschft. f. Geburtsh. u. Gynäk. 1901. 45.

Kermauner. Hegar's Beitr. 18. No. 2. (Believes that in fetal life certain cells undergo coagulation necrosis and the defects which arise depend upon the period in fetal development at which the necrosis occurred.)

49. Chrobak, R., u. v. Rosthorn, A. Die Missbildungen der weiblichen Geschlechts organe. Nothnagels Path. u. Therapie. 1908. 20, ii. Hölder, Wien., p. 194.

Bell, W. Blair. Jour. Obst. and Gynec. Brit. Emp. 1912. 21 : 209. (Claims that in imperforate "hymen" in 60 per cent of cases the membrane is of müllerian or wolffian origin because its inner side is covered with columnar epithelium. (?) In many cases the hymen is found on the outer surface of the membrane. See Eden and Lockyer, l. c. 1 : 314.

49b. Luer. Inn. Diss. München, 1903. Abst. Zentralbl. f. Gynäk. 1903. No. 27. (In a 40 cm. fetus complete atresia of middle third of vagina. There was absence of bladder and urethra.)

50. Vitrac. (Congenital hydrometrocolpos.) Rev. Mens. d'Obst et Gynéc. 1900. Ann. III, T. 2: 110.
51. Bulius. Verhand. d. X Gynäk. Kongress zu Giessen. 1901. 501.
52. Thompson. Ann. de Gynéc. 1885. T. 23: 143.
53. Ostermann. Zeitschft. f. Geburtsh. u. Gynäk. 28.
54. Odebrecht, E. Zeitschft. f. Geburtsh. u. Gynäk. 1896. 34: 535. Diskussion zu Nagel-Veit's Vortrag.
55. v. Neugebauer, F. L. Zur Lehre von den angebornen u. erworbenen Verwachsungen u. Verengungen der Scheide, etc. Berlin, 1895.
56. Williams, J. W. Johns Hopkins Hospital Report. 3: 85.
57. Kaufmann. l. c. (15). 2: 1040. (Autopsy of girl of 15 years with pulmonary tuberculosis and small caseating area in uterus with diffuse miliary tubercles of upper vagina.)
58. Springer. Zeitschft. f. Heilk. 1902.

Bierfreund. Zeitschft. f. Geburtsh, u. Gynäk. 15: 425. (Primary

lung tuberculosis, two ulcers near introitus, rest of pelvic organs free.)
59. JONES. Am. Jour. Obst. 1886. 265.
60. FRIEDLANDER, C. Lokale Tuberculose. Samm. Klin. Vort. No. 64, p. 518, resp. 4. (Portio and vagina, apparently primary.)
61. CATUFFE. Bull. Soc. Anat. de Paris. 1876.
62. EMANUEL. Zeitschft. f. Geburtsh, u. Gynäk. 29: 135.
63. ZWEIGBAUM. Zentralbl. f. Gynäk. 1888. 494.
63a. NEUMANN. Die Syphilis der Vagina, des Uterus u. seiner Adnexen. Muench. med. Wochenschft. 1895. Pp. 643, 684, 727, 774, 830.
WINTER. Lehrbuch d. gynäkologischen Diagnostik. S. Hirtzel. Leipzig, 1907. 352. (Gummatous ulcers and their differentiation from cancer.)
OPPENHEIM. Atlas der Venerischen Affektionen der Portio Vaginalis Uteri u. der Vagina.
64. BONNEY AND BRYDEN GLENDINING. Lancet. 1910. (Multiple cysts which they called "Adenomatosis vaginae." The cysts stained with mucicarmin and therefore were of cervical derivation (Aberrant cervical glands).)
65. WANNER, R. Zentralbl. f. Gynäk. 1912. 36: 1082.
66. PIQUÉ. Soc. de. Chir. 1898. 7: 6. (For this reason such cysts have been regarded by some as residua of hematomata, or mere collections of fluid in lymph spaces.)
67. FALKNER, A. Zeitschft. f. Geburtsh. u. Gynäk. 1903. 50, No. 3, 557.
68. GELLHORN. Zeitschft. f. Geburtsh. u. Gynäk. 62. Gynäk. Ges. Berlin.
69. PREUSSCHEN. Virch. Arch. 1877. 70: 111.
70. VEIT, G. Zeitschft. f. Geburtsh. u. Gynäk. 8.
71. MEYER, R. Arch. f. Mikr. Anat. u. Entwickungs. Gesch. 1909. 73. ("The Gärtner's ducts always run in the vaginal wall, never in the para-vaginal tissues." Therefore it is fair to assume that cysts developing from the duct will always have one surface close to the vaginal lumen, no matter in what direction they may further develop.—R. T. F.)
72. BUERGER, L. Traumatic Epithelial Cysts. Ann. of Surg. 1907. Aug. (Lit.)
72a. QUINBY, W. C. Some Urologic Aspects of Dermoid Cysts. Jour. Am. Med. Assoc. 1919. 73: 1045.
72b. CURTIS, A. See Surg., Gynec. & Obst. 1913. 16:715.
73. FREUND. Zeitschft. f. Geburtsh. u. Gynäk. 1.
74. CONITZER. Zeitschft. f. Geburtsh. u. Gynäk. 32: 293.
75. FREUND. Gynäk. Klinik. Strassburg. 1:321. Quoted by Veit, 3, i, 282.

76. NEEL, J. C. Calif. State Jour. Med. 1918. Nov. See also Gellhorn l. c. (68).
77. VASSMER. Arch. f. Gynäk. 60. (Lit.)
78. GUDER. Ueber Geschwülste der Vagina als Schwangerschafts u. Geburts Komplikation. In. Diss. Bern. 1889. (Sixty cases in all, including 23 cysts, 18 fibroids, 14 carcinomata, 4 hematomata.)
79. FRANK, R. T. Am. Jour. Obst. 1915. 72: 467. There were three cysts, one the size of a grape fruit, one orange, and the other walnut in size. The cysts had fibromuscular lining. I interpret them as derived from Gärtner's duct.
80. CULLEN, T. S. Bull. Johns Hopkins Hospital. 1905. 16: 207.
81. STOKES, J. E. Johns Hopkins Hospital Reports. 1899. 7: 109.
82. KIESSELBACH. Monatschft. f. Gynäk. 1912. 36: 404.
83. SCHMAUCH. Zeitschft. f. Geburtsh. u. Gynäk. 1900. 42.
84. BIDONE. Soc. ital. di ost. e gin. Ott. 1894.
85. SMITH, R. B. Am. Jour. Obst. 1902. 45: 145.
86. PATEL. Rev. de Gynéc. Chir. Abd. 1903. May, June.
86a. MÜLLER. Arch. f. Gynäk. 1914. 102:511. (Literature of 112 cases.)
87. LITTAUER. Centralbl. f. Gynäk. 1902. 26: 1406.
88. HASENBALG. Zeitschft. f. Geburtsh. u. Gynäk. 23: 52.
89. The following are cases of adenomyoma of the vagina.
MORALLER. Muench. med. Wochenschft. 1907. 1345.
AMANN. Gynäk. Ges. Muenchen. 1910.
90. HOFMOKL. Wien. Med. Presse. 1891. 1229.
91. MERKEL. Muench. med. Wochenschft. 1902. No. 13.
92. BROUN, L. Am. Jour. Obst. 1919. April.
93. General statistics: Of 59,600 female patients, 114 had primary vaginal cancer, or 0.19 per cent. Gurlt (Langenbeck's Arch., 25: 446). Williams, R., found 0.43 per cent of all carcinomas were vaginal. Schottländer u. Kermauner, l. c. (107) p. 659, puts them at 3.5 per cent of cancer of uterus and vagina; at from 0.2 to 0.4 per cent of genital carcinoma.
94. EPPINGER, QUOTED BY DÖDERLEIN, A., U. KRÖNIG, B. Operative Gynäkologie. G. Thieme. Leipzig, 1905. P. 504. (In 79 cases of uterine cancer, the vagina was involved in 35 cases. This was autopsy material.)
95. SCHLUND. Ueber das primäre Karzinom der Vagina, Sammelreferat über 273 Fälle. In. Diss. Freiburg i. Br. 1913. See Zentralbl. f. Gynäk. 1913. 862.
BROUN, L. Am. Jour. Obst. 1902. 45: 706. Taylor, H. C. Am. Jour. Obst. 1906. 54:860; Menge, Muench. med. Wochenschft. 1906. 53: 30; (New cases primary carcinoma vagina).
96. FALK. Gynäk. Ges. Berlin. 1911. 9/2. Zeitschft. f. Geburtsh. u. Gynäk. 1912. 68: 776. (A secundipara of 19 years; carcinoma

noted 4 weeks post partum, palliative treatment. Metastases in lungs, perforation of rectum.)

96a. WARD, G. G., JR. Post Graduate. 1908. Good literature.

97. v. WINCKLE, QUOTED BY EWING. Neoplastic Diseases. 544.

98. DÖDERLEIN U. KRÖNIG. l. c. (94) p. 505. (Of 123 cases from the literature they found the following: posterior wall, 71; anterior, 23; lateral, 13; circular diffuse, 16 cases.)

99. As Frankl, l. c. (23) p. 258, justly emphasizes, absolute certainty exists only when there is an intact area between the vaginal cancer and the cervix as in his Fig. 103.

100. LEGUEU. Soc. de Chir. 1907. 2: 13. (Only partial removal of vagina, still free from recurrence after 10 years.)

101. MALY. Centralbl. f. Gynäk. 1903. No. 27.
SCHLUND, l. c. (95) was able to find only 14 cases.

102. SCHLUND, l. c. (95) reports 17 cases.
FLECK. Arch. f. Gynäk. 64, No. 3.
v. SCHMIDT. Hygiea. 57: 555.

103. v. FRANQUÉ. Zeitschft. f. Geburtsh. u. Gynäk. 1907. 60.
BUTLIN. Brit. Med. Jour. 1909. Dec.

104. HIRSCH, G. Zeitschft. f. Geburtsh. u. Gynäk. 1911. 69: 742.

105. ARGAND ET PIOLLET. Rev. de Chir. 1911. No. 8. (Place aberrant cervical glands as etiological factor.)
POLLOSSON ET VIOLET. Ann. de Gynéc. 32, II, 675.

106. TAYLOR. Primary epithelioma. Am. Jour. Obst. 1906. Dec.

106a. JELLET, H. Jour. Obst. & Gynec. Brit. Emp. 1907. 12: 285.

107. SCHOTTLÄNDER, J., U. KERMAUNER, F. Uterus carcinoma. Berlin, 1912. Karger, p. 425. (In 134 cases of cervic cancer 45 per cent extended to the vagina. These extensions are usually of the squamous type, only 7 adenocarcinomata extending into the vagina.)

108. MILNER. Arch. f. Chir. 1904. 74: 669 and 1009.
CULLEN, T. S. Cancer of the Uterus. W. B. Saunders, Phila., 1909. 414. (Considers the vaginal metastases due to retrograde embolism. The uterine cancer was recognized only one year later.)

108a. HELLENDAL, H. Hegar's Beitr. zur Geburtsh. u. Gynäk. 1902. 6. (Lit.)

109. SEMMELINK, H. B. Nederl. Tijdschr. v. Verlosk en Gynec. 1898. 9. (After ovariotomy metastasis in vagina.)

110. LEISEWITZ. Demonstr. Gynäk. Ges. Muenchen. 1904. Oct.

111. LAUENSTEIN. Muenchen. med. Wochenschft. 1895. 407.

112. McFARLAND, J. Sarcoma of the Vagina. Am. Jour. Med. Sc. 1911. April.

113. BLAND, P. B. Jour. Am. Med. Assoc. 1912. 59: 509.

114. JELLET AND EARL. Jour. Obst. & Gynec. Brit. Emp. 1904. 230. (Of 39 cases of primary sarcoma, only 2 were of the diffuse type.)

SEITZ, O. Ueber primäres Scheidensarkon Erwachsener (Lymphendothelioma). Samm. Klin. Vort. 1900. No. 28. (Of 29 sarcomas, 12 were spindle-cell variety.)
115. SPIEGELBERG. Arch. f. Gynäk. 1872. 4.
116. v. ROSTHORN. Wien. Klin. Wochenschft. 1899. No. 38.
117. KLIEN. Monatschr. f. Geburtsh. u. Gynäk. 1898. 7: 581.
118. KAUFMANN. l. c. (15) 1041.
119. BOLDT. Am. Jour. Obst. 1906. 54: 550.
GRAEFE, M. Monatschr. f. Geburtsh. u. Gynäk. 1912. 35: 196.
120. HOFMOKL. Wien. Med. Presse. 1891. 1229. (Case described as primary but really metastasis of uterine.)
121. WILMS, M. Die Mischgeschwülste Heft, 2. Die Mischgeschwülste der Vagina u. der Cervix uteri. Leipzig, 1900.
122. VEIT. l. c. 21, 3, i, 298.
123. AHLFELD, I. F. (Botryoid sarcoma in girl of 15 years.) Arch. f. Gynäk. 1880. 16:135.
SIMMONS. (Botryoid sarcoma in girl of 19 years.) Trans. Edinb. Obst. Soc. 1884–5. 10: 205.
124. D'ARCY POWER. Lancet. 1895. 2: 984.
125. DEMME. Bern Jennerischem Kinderhosp. 1892. 19: 95.
126. SCHUCHARDT, K. Virch. Arch. 1889. 117: 262.
127. SOLTMANN. Jahresbericht. f. Kinderheilk. N. F. 17.
128. KOLISKO, A. Wien. Klin. Wochenschft. 1889.. 2: 119. (Three cases each containing striped musculature. Piquand, Rev. de Gynéc., 1905, 579, says that the muscle cells as found in this class of tumor resemble those of a fetus at three months.)
129. PICK. Arch. f. Gynäk. 1894. 46: 191. (Literature.)
130. PERNICI. Virch. Arch. 113.
131. HAUSER. Beitr. z. Allg. Pathol. u. Path. Anat. 1903. 33.
132. KALUSTOW. Arch. f. Gynäk 40: 499.
133. KOERNER. Quoted from Veit's Handbuch. 21, 3, i, 302.
134. HURDON, KELLY AND NOBLE. L. c. 1: 101.
135. ISRAEL-HOLLÄNDER. See Pick, L. Arch. f. Gynäk. 46:191.
MEYER, R. Lubarsch Ostert. Ergeb. 1905. 9, ii, 518.
PUECK ET MASSABIAU. Ann. de Gynéc. & Obst. 1908. 2s, 5:306. (Botryoid in old person.)
136. GELLHORN, G. Am. Jour. Med. Sc. 1918. 156: 94.
136a. CHANDLER, A. S. Animal Parasites and Human Disease. John Wiley & Son. New York, 1918. 278.
137. DE LEE, J. B. Trichimonas vaginalis vaginitis. Illinois Med. Jour. 1920. March.
137a. NEUMANN, R. O., AND MEYER, M. Lehmann's Med. Atlanten, 11, Wichtige tierische Parasiten u. ihre Uberträger. München, 1914. 22.

138. HORWOOD. Brit. Med. Jour. 1906. March 10. (Polypoid tumor of cervix due to Bilharzia.)

MILTON. Loos Handbuch der Tropen Kranheiten. (Acute vaginitis due to Bilharzia.)

139. Rhabditis Pellio (a nematode) in the vagina. See Fantham, Stephens and Theobold, Animal Parasitology of Man. Wm. Wood. 1916. 377.

140. Anguillulo aceti, "vinegar eel," may be found in vaginal secretion after vinegar douches.

TODD, J. C. Clinical Diagnosis. W. B. Saunders, Phila. & London, 1918, 4th Edition, p. 237.

CHAPTER VII

THE UTERUS

I. CHANGES IN SIZE AND POSITION OF THE UTERUS AND VAGINA—PROLAPSE, MALPOSITIONS

The physiological changes, which include descent of the uterus into the pelvis during late fetal life and infancy, growth during childhood, the changes incident to puberty, to the menstrual cycle, pregnancy, and to senility, have been described in Chapters III and IV.

Temporary changes of position due to differences in fullness of bladder and rectum, of posture (prone, standing), of intra-abdominal pressure, are kept within physiological limits by the suspensory or holding apparatus (fascia, ligaments, etc.) and the supporting apparatus (musculature, pelvic diaphragm).

The theme of the present discussion deals solely with changes due to abnormal influences. As both the causes and the resulting diseased condition almost invariably affect the vagina and uterus simultaneously, it is expedient to discuss most of them together.

1. **Vagina.**—*Reduction in size* results from causes mentioned under atresia and stenosis (p. 143), senile changes and pressure of tumors from without.

Dilatation of the vagina is produced by vaginal tumors or intra-uterine or cervical growths projecting into its lumen, by accumulation of fluid behind an imperforate hymen or an atresia. A passive dilatation due to loss of tone results from birth injuries.

Lengthening of the vagina is due to any cause which pulls the uterus upward and fixes it in an elevated position, such as large fibromyomata, massive intraligamentous cysts. Causes which dilate the vagina may also lengthen it (vide ante).

2. **Uterus.**—*Abnormal smallness* may be due to congenital hypoplasia, to transient hypofunction of the ovaries, lactation atrophy, wasting disease, endocrine disturbances (as hyperpituitarism), to castration atrophy.

Enlargement of the uterus may be due to premature sexual development in children. It regularly results from multiparity. Chronic stasis causes increase in size—passive congestion of heart disease, retroflexion, prolapse. A low grade of chronic inflammation (myometritis), tumors, distention of the uterine cavity likewise cause enlargement.

Dilatation of the uterus may follow upon vulvar, vaginal or cervical

atresia. The fluid may be mucus, blood or pus. Development of a submucous tumor may distend the uterine cavity. The muscular walls may be greatly thinned out, in other cases a concentric hypertrophy results.

Versions.—Changes of relation of the long axis of the uterus as a whole, to the vagina. Ante, retro, and lateroversion can occur. Of greatest importance is retroversion, in extreme degrees of which the fundus may lie in Douglas's cul-de-sac.

Positions.—Ante, retro and latero positions are recognized. The uterus is displaced in the direction indicated without changing its relation to the vagina. Ante position commonly results from displacement by masses in the posterior cul-de-sac. Retroposition is most frequently due to shortening of the sacro-uterine ligaments as a sequel to inflammation. Unless the uterus is firm, a flexion rather than a displacement results.

Flexions.—Anteflexion, the uterine body bent forward, is the normal position, unless fixed by adhesions, tumors or exudates. Retroflexion not infrequently is congenital. It is acquired most often during the puerperium, at which time softness of the involuting organ and the dorsal posture combine to produce this displacement. Retroflexion is backward displacement of the fundus. Clinically, this is most important, as it favors the development of prolapse. Lateroflexion, either dextro or sinistro, is bending to one or the other side. The apex of the angle in these conditions is at the level of the internal os.

Incarceration of the Uterus.—A retroverted or retroflexed uterus enlarging during pregnancy may become incarcerated. More often the adhesions causing the malposition soften and give way, allowing spontaneous elevation; in other cases abortion takes place. In a small number, due to strong fixation, a projecting promontory, tumors, etc., the incarceration is not relieved. Acute symptoms develop in the fourth month. Exfoliative cystitis, hydronephrosis, perforation of the bladder and ileus have been observed (Duhrssen, 1).

Elevation of the uterus occurs normally in pregnancy. It may result from masses in the pelvis lifting the uterus from below (hematocele, hematocolpos, exudates, tumors in the cellular tissues); from enlargements by tumor of the uterus or organs in juxtaposition raising it, when the pelvis can no longer accommodate their bulk; from adhesions to the abdominal wall or other viscera acquired during the later months of pregnancy and persisting after labor.

3. **Prolapse of Uterus, Cystocele, Rectocele.**—Prolapse, if not used in its most limited sense, may include simultaneous descent of the uterus, bladder, rectum and vagina. It is also employed in reference to the descent of individual organs, as cystocele, or prolapse of the bladder; rectocele, or prolapse of the rectum.

The means by which the pelvic organs are kept in place, the injuries and the mechanisms involved in their descent, have given rise to prolific discussion and have

inspired an enormous literature. Only a few authors will here be referred to. Halban and Tandler, (2) in a monograph beautifully illustrated, express the conviction that the pelvic diaphragm, i.e., the levator ani and its associated muscles, are the essential factor in keeping the uterus in place. E. Martin (3), in an equally thorough study, concludes that the connective tissue situated between the levator and the peritoneum affords the main support. In the writer's opinion, shared by others (Frank, Liepmann, 4), an intermediate viewpoint is the correct one. Halban (4a) has lately also modified his views. A brief exposition of the normal anatomy, of the factors producing prolapse, and the varieties of prolapse, is all that can be attempted in a book of this character.

Anatomy.—The bony pelvis is incomplete. The gap is closed by certain tissues found between the pelvic peritoneum which bounds the abdominal cavity and the skin surface of the mons, vulva, perineum and peri-anal region.

Upon removing the peritoneum, the subperitoneal space which extends to the levator ani is exposed. Here the uterus from above the level of the internal os is found projecting from a mass of connective, areolar and unstriped muscle tissue (Fig. 116), of which different parts have received different names. They all radiate from the uterocervical junction as a center. The lateral portion marked "P," which is also the strongest and best developed, is known as the parametrium (Cardinal ligaments, Kock's transverse ligament, 5), where it attaches to the uterus, and as paracolpium where associated with the vagina. This mass of tissue runs from the cervix and vagina and spreads out fan-shaped onto the pelvic wall. The posterior part extending from cervix to each sacro-iliac synchondrosis, surrounds the rectum. These strands are known as the sacro-uterine ligaments and form the lateral edges of the cul-de-sac of Douglas (Fig. 116). Anteriorly, between the posterior surface of the pelvic bones and the cervix, courses a thinner layer, reinforced on each side of the median line, and known as the pubocervical ligaments (Figs. 116 and 117).

The space between peritoneum and pelvic diaphragm additionally contains the ureters, blood vessels, nerves and lymphatics, and also the bladder and rectum, whose relations will shortly be described.

The pelvic diaphragm is composed, when looked at from within (that is from above), after removal of all superimposed structures, of a bowel-shaped muscle plate (Fig. 118).

This musculature derives its origin anteriorly from the posterior surface of the pubic rami, and from there to the ischial spine, from the white line (arcus tendineus) and aponeurosis of the obturator internus. The fibers course along lateral to urethra and vagina and insert anteriorly into the anterior and lateral walls of the rectum (puborectal fibers), and behind the rectum unite with the muscle of the opposite side to form a median raphe as far back as the coccyx. The triangular coccygeus muscle completes the diaphragm on each side behind the levator.

The oval gap, some 3 to 4 cm. in width, left between the anterior rectal wall and the pubis, bounded on each side by the puborectal fibers, has aptly

FIG. 116.—DISSECTION OF FEMALE PELVIS SHOWING SUBPERITONEAL CONNECTIVE TISSUE. *p* showing connective tissue of pericolpium and around cervix (base of broad ligament). *r.u.* Bottom of recto-uterine pouch (cul-de-sac of Douglas). *o.i.* Cross section of uterus at internal os. *v.u.* Bottom of vesico-uterine pouch. (From E. Martin.)

FIG. 117.—PHOTOGRAPH OF CADAVER DISSECTION SHOWING UTERUS, BEGINNING OF URETHERA (1), PUBOCERVICAL LIGAMENTS (2), AFTER REMOVAL OF BLADDER.

been called the *hiatus genitalis.* This gap receives reinforcement from the triangular ligament below the primary diaphragm (Fig. 119).

Looked at from below after removal of the skin and vulva, the *triangular ligament* or *accessory pelvic diaphragm* can be demonstrated as a thin but strong structure composed of two fascial layers enclosing the deep transversus perinei muscle. It ends midway between fourchette and anus in the center of the perineal body (Fig. 120). It is pierced by the urethra and vagina.

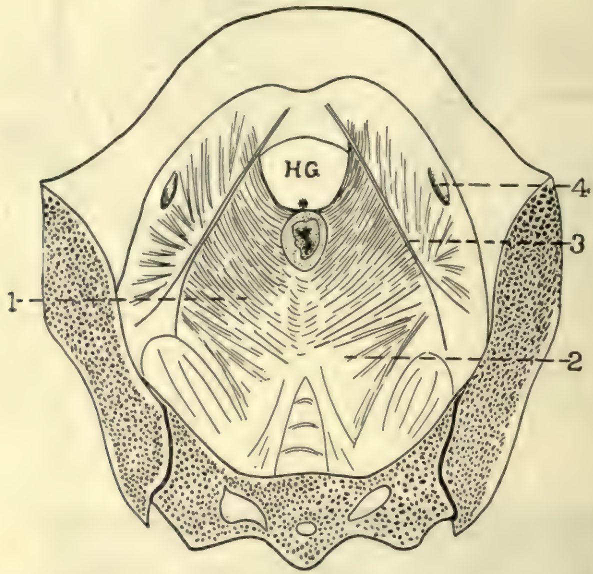

FIG. 118.—PELVIC DIAPHRAGM OF A NULLIPARA VIEWED FROM WITHIN. After removal of all viscera except that portion of the rectum which pierces the levator muscle. (H.G.) Placed within the sharply defined "hiatus genitalis" which is foreshortened by being viewed from above and behind. The asterisk designates site of central tendon of perineum. Behind asterisk is the rectum cut across. The muscle fibers bounding the lateral margins of the hiatus are the pubo-rectal portion of the levator ani muscle. 1. Ischial portion of levator forming median raphe with muscle of opposite side. 2. Coccygeus muscle. 3. "White line" or arcus tendineus. 4. Obturator canal, piercing obturator internus muscle. Compare with next figure which shows structure closing hiatus genitalis, also viewed from within. (Modified from Halban and Tandler.)

The fascia which covers the levator ani, and which also helps to form the superior layers of the triangular ligament, is the parietal layer of the endopelvic fascia, which lines the entire abdominal cavity. Every structure passing through the fascia receives an investment which runs both upward and downward. In this instance the urethra, the vagina and rectum each receive such fascia, which are known as their *fascia propria.*

The majority of anatomists prefer to describe the fasciae of the pelvis as composed of a parietal layer (transversalis fascia, obturator, levator, etc., fascia) and of a visceral

layer which divides into endovesical, vaginal and rectal fasciae. This division is certainly not feasible in operative work nor are the layers demonstrable in the fresh cadaver. For details of anatomical description see Poirier and Charpy (6), Webster (7) and Waldeyer (9).

At the edge of the puborectal fibers, i.e., the edge of the genital hiatus, the pelvic fascia (here known as the levator ani fascia) turns and becomes continuous with the fascia covering the outer surface of the levator muscle, known as the anal fascia (Fig. 122). From inside the pelvis this edge is not seen in the undissected state as the triangular ligament is fused with it. From Fig. 120 it becomes apparent that along the levator edge five fascial

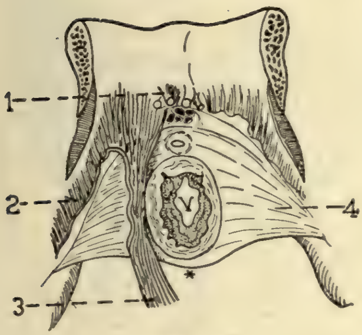

FIG. 119.

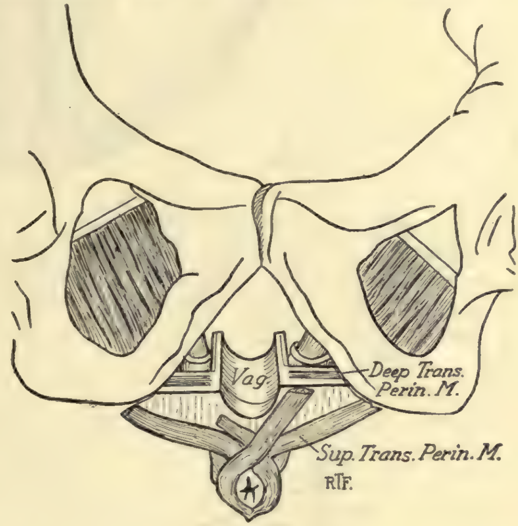

FIG. 120.

FIG. 119.—STRUCTURES BEHIND AND BELOW THE PUBIC ARCH. Shows relationship of superior layer of triangular ligament (4) to the urethra and vagina (V) which pierce it. The pubo rectal fibers (3) of the levator ani course superior to the triangular ligament and lateral to the vagina. The Ischial portions of the levator (2) are cut away. (1) shows the attachment or origin of the pubo cervical ligament which supports the bladder, to the posterior surface of pubic bone. (*) marks the central portion of the perineum. (Modified from Savage.)

FIG. 120.—MODEL OF PELVIS AND PELVIC OUTLET. The triangular ligament has been cut across, in order to demonstrate the junction of five fascial planes. From without inward—Superficial layer of the triangular ligament, deep transverse perineus muscle, deep layer of the triangular ligament, junction of anal and levator ani fascia (rounded edge), fascia vaginae propria. The muscles superficial to the triangular ligament are also shown—Superficial transverse perineus, constrictor cunni.

planes meet and fuse. This is the main point of fixation for the lower third of the vagina.

Thus the lower aperture of the abdomen is partly bony, partly composed of soft parts. The cervico-uterine junction is the point from which the subperitoneal connective tissue (the holding apparatus, "retinacula" of

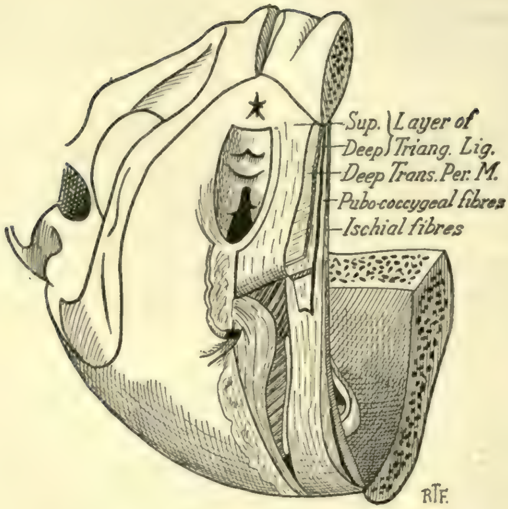

Fig. 121.—Anterior and lateral view of muscles and fasciae. The relation of the sphincter ani to the trianglar ligament and coccyx are shown. The various parts of the levator muscle appear—pubococcygeal sling; between it and the sphincter are shown the puborectal portion, and running transversely to the pubococcygeal fibers, the ischial part can be distinguished.

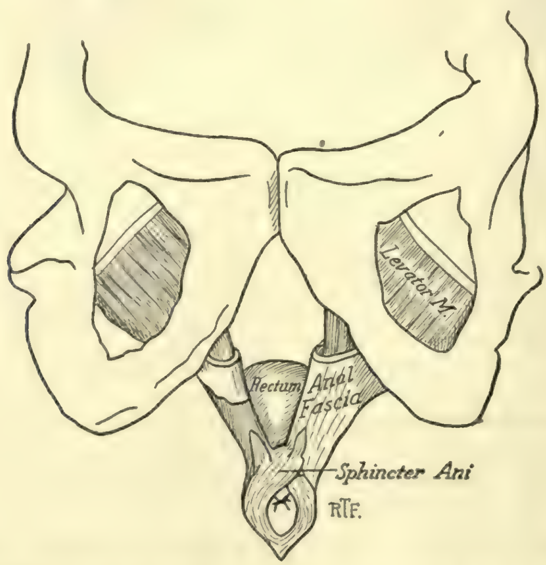

Fig. 122.—Nulliparous outlet, showing the two levatores ani approaching toward the rectum, the levator gap, the rounded edge of each muscle, and the fascial junction. The lower or outer fascia is called anal fascia, the inner fascia (only its edge is seen) is known as the levator fascia. The external sphincter ani appears.

Martin) radiates to the pelvic wall. This elastic sling permits excursions of the uterus in all directions in response to changes of intra-abdominal pressure or distention of neighboring viscera. When the pressure ceases the uterus is passively pulled back.

The pelvic diaphragm (supporting apparatus of Halban and Tandler) (Fig. 118) is a musculofascial plate which both reflexly and in response to the will, by its contraction narrows the genital hiatus and absorbs shocks due to increased abdominal pressure.

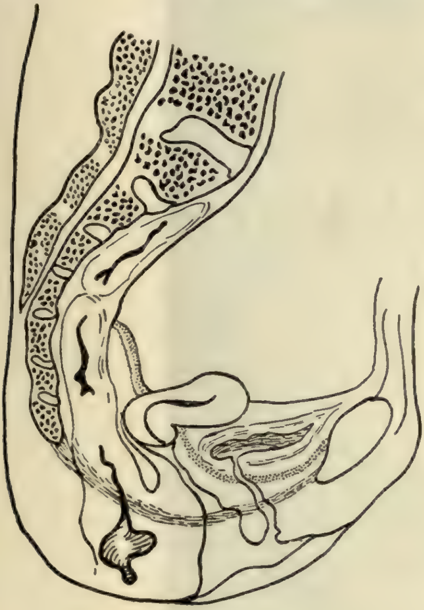

FIG. 123.

FIG. 124.

FIG. 123.—EXTRA MEDIAN ANTERIO POSTERIOR SECTION SHOWING RELATIONSHIP OF THE MUSCULAR DIAPHRAGM (LEVATOR SLING) TO BLADDER, UTERUS AND RECTUM. Levator muscle is shown in broken lines; sacro-uterine ligament and pubocervical ligament in fine dots. (Modified from Crossen's Operative Gynecology.)

FIG. 124.—MULTIPAROUS OUTLET. The wide levator gap due to stretching and tearing of the levator muscles and fasciae is shown, also bulging rectum due to tear of fascia recti propria. On the left the anal fascia has been almost entirely removed, on the right junction of levator and anal fascia along the edge of the puborectal fibers is plainly shown.

"The holding apparatus may fitly be compared to the springs which continually maintain the burden, and the supporting apparatus to the shock absorbers which ease exceptional stresses and strains" (4).

From a practical point of view, though not according to exact anatomical criteria, the bladder lies not only above the triangular ligament but also above the holding apparatus (in its case the pubocervical fascia) (Fig. 117). The urethra pierces both this fascia and the triangular ligament. That portion of the rectum devoid of mesentery, on the other hand, lies above the pelvic diaphragm but below or surrounded by the holding

apparatus, the periproctium, below the lowest level of Douglas's cul-de-sac (Fig. 123).

Pathology.—The trauma of childbirth may produce diverse injuries to the pelvic outlet. A sagittal tear in the pubocervial fascia allows the bladder to prolapse into the vagina and then to appear at the introitus beneath the triangular ligament. If the triangular ligament is also torn the

FIG. 125.—COMPLETE PROLAPSE OF UTERUS SHOWING EXTREME LAXNESS OF ALL TISSUES, HYPERPLASIA AND EDEMA OF CERVIX, DESCENT OF ANTERIOR RECTAL WALL.

more anterior portion of the bladder and part of the urethra will descend in response to intra-abdominal pressure (Hirst, 9).

Median tears of the perineal body need not be followed by rectocele if the fascia propria of the rectum is not torn. Conversely, with an intact perineal body, a large rectocele may protrude over the perineum if the fascia propria is torn above. Commonly, perineal tears and injury to the rectal fascia occur simultaneously. Injury to the puborectal fibers allows the anus to drop back (Fig. 124).

Complete tears of the perineum, or extensive tears are not necessarily followed by prolapse. If the genital hiatus is enlarged by multiparity and consequent injuries (Fig. 124), greater demands are made upon the holding apparatus, which it successfully bears in many instances. In other cases, favored by stretching of the tissue during childbirth, relaxation consequent to general enteroptosis, retroflexion and version of the uterus, a gradual descent in the axis of the pelvis occurs through the vagina. Almost invariably the bladder prolapses with the uterus and upper vagina as the support of the pubo-cervical fascia is withdrawn. The rectum follows only if its fascia has been torn (Fig. 125).

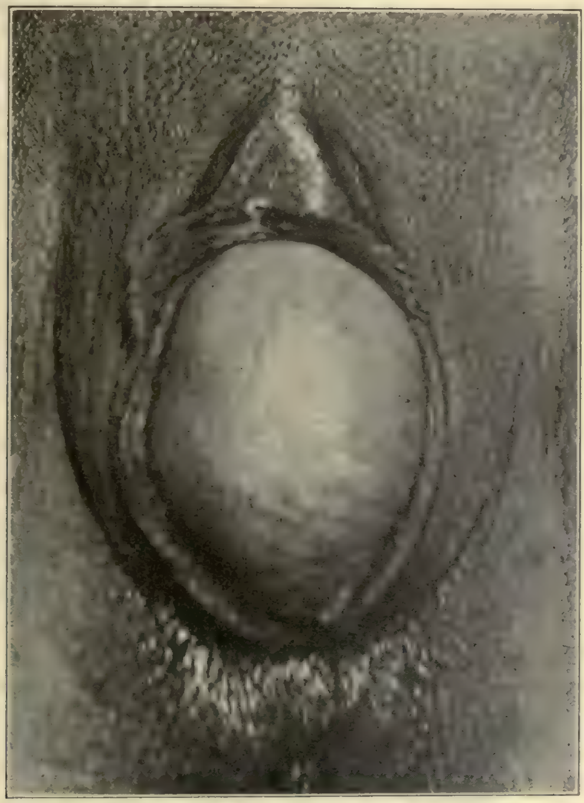

FIG. 126.—TRUE HERNIA OF DOUGLAS'S CUL-DE-SAC IN A NULLIPAROUS WOMAN WITH HIGH FIRM PERINEUM. The mass contains only little of the rectum, consists mainly of the posterior peritoneal pouch filled with ascitic fluid due to cirrhosis of the liver.

It will be noticed that in independent rectocele or cystocele the lower or caudal part of the vagina prolapses first; in primary uterine prolapse, the upper portion of the vagina initiates the process.

Prolapse in the Nulliparous.—Spina bifida (both overt and occult) can produce prolapse in the nulliparous and even in children (Ballantyne and Thompson, 10). Here injury to the fourth sacral nerve is supposed to paralyze the musculature. On the other hand in infantilism (Kepler, 11), enteroptosis, extreme lordosis, etc. (Rosenthal, 12), in response to sudden

strains, prolapse of the uterus through an intact hymen has been observed, the musculature apparently functioning normally (Frank, 13).

Changes Subsequent to Prolapse.—In all degrees of prolapse, in consequence of exposure of the mucous membrane to the desiccating influence of the air, dryness, brittleness, excoriation and epidermoidalization may result, the frequent trauma incurred favoring decubital ulcers.

Carcinoma of the cervix in prolapse is rare. Five cases were reported at the 1919 meeting of the American Gynecological Society (13a). The cervix is almost invariably

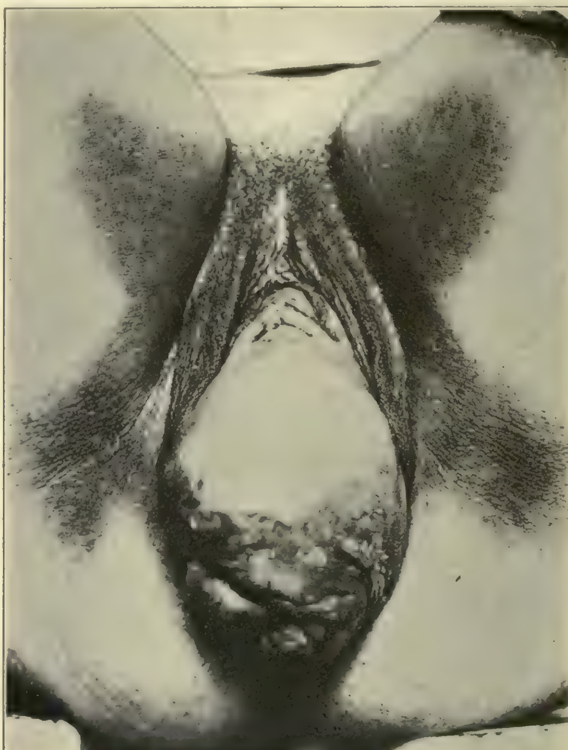

FIG. 127.—COMPLETE PROLAPSE SHOWING ON THE LEFT SIDE A DEEP LACERATION OF THE CERVIX; THE POSTERIOR LIP SHOWS A DECUBITAL ULCER; EDEMA OF THE CERVIX; ENORMOUS CYSTOCELE WITH BLADDER DESCENDING DEEPLY ALONG RIGHT SIDE OF CERVIX.

swollen and edematous, its lips everted (ectropion). The edema may involve the everted vaginal and rectal walls as well, Fig. 127. In rare instances through excessive edema or through formation of intrapelvic adhesions a prolapse may become irreducible (13a Barbour-Simpson).

Preliminary to prolapse of the uterus an *elongation of the supra and infravaginal parts of the cervix* may take place. The uterine canal may measure 12 to 15 cm. in length. The increase results from the continued hyperemia, aided by the traction of a large vagina, in cases in which the

levator and muscle elements are torn but the fascial supporting structures are intact. Fixation of the fundus by adhesions, etc., favor the process. (Kelly and Noble, l. c. I, 424). Hirst (l. c. 318) has seen three cases of firm ventrofixation in which the vagina prolapsed and the enormously elongated cervix protruded from the vulva.

Prolapse may develop *secondarily* independent of the trauma of childbirth or of spina bifida, in consequence of the pressure exerted from above by a large tumor, massive ascites or pseudomyxoma of the peritoneum. Upon removal of the cause the genital organs may resume their normal position. The immediate return may be very strikingly seen after paracentesis abdominis.

Injuries occurring in prolapse have been described (p. 172). Pregnancy in a prolapsed uterus is not infrequent. After the fourth month the enlarged body of the uterus retains that organ above the pelvic brim. Except for increased incidence of abortion, and danger of infection from decubital ulcers, no unusual conditions develop (Anderodias, 13c). *Hernia,* especially inguinal, is not infrequent, as childbirth and laxity of the fascial planes favor both conditions. Mayer's statistics of 40 inguinal herniae in 293 cases of prolapse far exceed the proportion usually noted (13d). *Prolapse of the rectum* occasionally accompanies prolapse of the uterus, the uterine prolapse being much more frequent than rectal descensus.

Vaginal Enterocele (hernia through Douglas's cul-de-sac; anterior enrocele; pudendal hernia, perineal hernia).

Posterior enterocele is the more common (Mayer, 13d). It is favored by congenitally deep cul-de-sac, but in most instances a tear of the recto-uterine fascial plane first allows a hernial evagination of the peritoneum between vagina and rectum (Frank, l. c., 13) (Fig. 126). The mass may bulge into the vagina or, in extreme cases, appear in the perineum (Sweetser, 14). If Moschcowitz's (14a) conception of prolapse of the rectum is correct, enterocele always accompanies descent of this viscus. Veit (Veit's Handbuch 3:336) believes that a previously existing exudate plays a rôle in weakening the pelvic diaphragm at the neck of the sac.

Anterior enterocele has been described by Kelly (15). The intestine may force its way along the vesicovaginal septum or pass along the lateral vaginal wall into the labium majus.

Under the misnomer of *pudendal hernia* (Moschcowitz, 15a), or hernial protrusions appearing in the posterior portion of the labium majus, eleven cases, all occurring in females, have been described. The hernia escapes from the abdomen through a rent in the levator ani and its fasciae, immediately behind the symphysis pubis—subpubic hernia (v. Winckel (15b)), and reaches the labium, after passing alongside the vagina, through the triangular space bounded by ischiocavernosus, constrictor cunni and transversus perinei. The trauma of difficult labor has been the usual cause.

Perineal hernia of which Moschcowitz (16) finds 28 cases, usually makes its exit through the potential cleft between levator ani and coccygeus muscles or through the posterior fibers of the levator. The protrusion appears in the perineum behind the

transversus perinei or in the ischiorectal fossa. This author's case was in a female 2½ years old.

Hysterocele.—The uterus may be found as the content of a hernia. Usually one or both adnexa are also in the sac. Femoral hysterocele is the most unusual, inguinal the most frequent. Hernia through an abdominal scar and true umbilical hernia are on record. Birnbaum (17), Andrews (18) found the nongravid uterus involved 43 times, the gravid one, 30 times. In pregnancy, abortion during the third to fourth month is the rule, but delivery at term after reduction by taxis or cesarean section has been performed (Eisenhardt, 19). So frequently do anomalies of development, especially uterus didelphys occur in cases of hysterocele, that some predisposition must be thought of. Neugebauer (20) found the uterus in the inguinal canal in 14 cases of pseudohermaphroditism masculinus. Blair Bell removed the two uterine bodies of a didelphic uterus, from opposite inguinal hernia sacs (20a).

Inversion of the uterus is partial when the fundus invaginates into the body, complete when the body has invaginated through the cervix and the entire inverted organ, dragging the inverted vagina with it, has prolapsed through the vulva. Intermediate gradations occur (Kaufmann, 20b). Inversion usually is a postpartum complication taking place in the third stage (Crampton, 20c) of 224 cases, 196 immediately post partum, only 11 occurring later than 11 hours after birth of the child.)

It is infrequent in hospitals (3 times in 51,290 cases in the Glasgow Maternity, Kerr, 21), but more frequent in private cases—in two years Kerr was able to find 23 cases in the literature. Inversion may occur after abortion. It has happened as late as two weeks post partum (De Lee, 22). Adherent placenta, unskillful manipulation (such as too forcible Credé's expression, traction on the cord (Vogel, v. Jaschke, 23), short cord, attacks of coughing, straining, if simultaneously relaxation of the lower uterine segment occurs, may be causative. Hypoplasia of the adrenals has been regarded as causative (Mansfeld, 23a). The accident is slightly more frequent in primiparae (Vogel, 23). Death takes place in from 14 to 18 per cent (Kerr, 21; Beckman, 24), from shock, hemorrhage or sepsis. If unreduced, *chronic inversion* may result with epidermoidalization of the exposed endometrium, which, after reduction, may yet reconstruct and permit of renewed pregnancy (Schauta, 24a).

In the non-pregnant state the traction of tumors on the fundus may produce inversion (submucous myoma—Kelly and Cullen, 25), spindle-cell sarcoma (Kelly), malignant tumors (Schoenig, 25). The condition is uncommon as compared to its occurrence in pregnancy (1:9 Veit's Handbuch, l. c. I, 386).

The exposed mucous membrane bleeds immediately after the accident. Later it is covered with exudate, and then granulation tissue forms. Involution may take place and reduction to the normal non-pregnant size. Per vaginam the tubal openings can be seen and per abdomen an "inversion funnel" into which the fallopian tubes extend and from which the ovaries

project, can be felt. Histologically, the glands of the mucosa diminish in number, squamous epithelium may replace the surface covering, round-celled infiltration and hyaline degeneration of musculature are noted (Caruso, 26).

Fullerton (27) reported three cases of uterine inversion after onset of the menopause. In two, prolapse of the uterus existed previously.

Taylor (28) saw a case in a virgin of 18, no tumor of the uterus existing. Reimann (29) in 64 cases of *birth of the child post mortem,* found a record of seven inversions. Accumulation of gas in the intestine which probably produces expulsion of the child, also causes the uterine inversion.

Torsion of the uterus is a rotation of the entire organ as a whole on a vertical axis, or rotation of the body on the immobile cervix. A slight degree of rotation commonly toward the right, is an almost constant occurrence during the later months of pregnancy (requiring consideration in making the uterine incision in cesarean section) (Glinski, 29a).

Tumors of the uterus, especially fibromyomata (Kelly and Cullen, 30), ovarian cysts (Masmonteil, 30a), and fibrous bands (Fowler, 31) may produce it. Complete separation of body from fundus has been recorded. Mazzini (31a) reports a case in which the gravid half of a uterus didelphys became twisted, causing apoplexy of the uterus.

Some, as Küstner (Veit's Handbuch, l. c. 1, p. 113), distinguished between "rotation" in which cervix and corpus turn as one, and "torsion" in which the cervix remains immovable, the body alone turning. The distinction does not appear important nor is it always possible to demonstrate these subvarieties.

4. Circulatory Disturbances.—Circulatory disturbances in the uterus show themselves in a different fashion than in other portions of the genital tract, because of the fact the periodic bleeding is a uterine function throughout the years of sexual life. This bleeding, as has been shown in Chapter IV (p. 79), is part of the regressive process which results if the ovum for which the uterus has prepared a nidus, fails to be impregnant. Each healthy woman has a periodicity, which varies within the general limits given as normal; similarly the quantity of menstrual blood differs in different individuals. Marked increase in the usual amount is called *menorrhagia;* when the bleeding loses its periodicity occurring at times not corresponding to the cycle, it is referred to as metrorhagia (32).

There are varieties of uterine hemorrhage which *eo ipso* have no connection with the uterine function—such as bleeding from injuries, erosion of vessels by tumors, etc., which, however, until their etiology is established, are necessarily classed with metrorrhagia.

As bleeding is a function of the uterus, absence of menstruation, *amenorrhea,* is a circulatory disturbance and will be discussed in this connection. Bleeding during pregnancy, at which time amenorrhea is physiological, likewise requires mention.

1. Hyperemia.—Aside from the physiological hyperemia of menstruation and pregnancy, the uterus is hyperemic in the majority of conditions referred to in the next paragraphs, because especially in the uterus, hyperemia favors hemorrhage. A marked degree of congestion results from prolonged coitus and coitus interruptus. Passive hyperemia may be due to

retroflexion and to tumors which impede the venous return by exerting pressure on the pelvic veins.

2. HEMORRHAGE.—Hemorrhage may be due to purely local, to ovarian, and to general systemic causes. After the onset of the menopause, intra-uterine bleeding and malignancy are almost synonymous.

Local Causes.—During the acute stages of uterine inflammations both menorrhagia and metrorrhagia occur, in consequence of capillary hyperemia. Bleeding may result in tuberculosis and syphilis from similar causes. Retroflexion in which the venous return is often impeded, can cause menorrhagia. Tumors, benign, such as fibroids, and polyps, which cause or are accompanied by great increase in vascularity, occasion both forms of bleeding. In malignant tumors direct erosion of vessels causes irregular hemorrhage. The bleeding resulting from trauma will, of course, likewise bear no relation to the cycle.

Bleeding during pregnancy is pathological. It may arise from detachment of the placenta during abortion, from polyps or erosions of the cervix (most frequently at four-week intervals corresponding to the suppressed cycle—pseudomenstruation), or from ruptured varices. During labor placenta previa and premature detachment of the placenta are the usual causes. Postpartum, injuries to the birth canal, failure of the uterus to contract, placental remnants, are among the frequent causes of hemorrhage immediately after labor. Subinvolution, placental polyps, chorioepithelioma may produce bleeding during the puerperium.

Ovarian Causes.—An excess of chemical stimuli from the ovary produce hyperemia and bleeding. If long continued, hyperplasia of the mucosa and hypertrophy of the musculature supervene, producing the "metritic" uterus. In most cases the primary stimulus affecting the ovary is unknown. In some instances, endocrine disturbances (early stages of Basedow and acromegaly), in others, excessive sexual intercourse, over-activate the gonad, adnexal inflammation (Whitehouse, 33) and ovarian cysts with twisted pedicle, which produce acute changes in the output of the ovarian hormone or hormones, occasion uterine bleeding. In any or all of the above conditions, the mucous membrane may show hyperplasia, or may prove identical with a normal menstrual mucosa.

General Systemic Causes.—In acute infections diseases such as typhoid, typhus and smallpox, menorrhagia and metrorrhagia may occur. In blood diseases, examples of which are purpura, less frequently, hemophelia, in which the females more often escape (though transmitting the disease) uterine bleeding may be prominent (Fränkl and Bohm, 34). In circulatory decompensations with venous stasis, especially mitral stenosis (Gow, 35) and late stages of renal disease, in toxic conditions as phosphorus poisoning (Lewin and Breuning, 36), in severe nervous disturbances resulting from fright, shock, acute manias, irregular or profuse bleeding may be noted.

In all of the conditions referred to, the bleeding takes place from the uterine cavity, in a few also from the cervix. In a small number of cases intraperitoneal hemorrhage of uterine origin occurs, for example, in rupture or perforation of the uterus and in rupture of subperitoneal varices.

3. AMENORRHEA or absence of uterine cyclical bleeding can hardly be regarded as a circulatory disturbance in *primary* conditions (i.e., where the function has never been established). Here it is a developmental deficiency.

Local conditions such as too radical curettage, atmokausis, prolonged radium treatment, pyometra, may cause permanent amenorrhea by destroying the endometrium.

Ovarian hypofunction, total after double oöphorectomy, partial after X-ray exposure, ovarian lesions of various kinds may occasion absence of menses.

General causes include wasting diseases, chlororis, unfavorable or sudden changes of environment, endocrine disturbances (myxedema, late stage of acromegaly).

Aneurism of the uterine artery has been observed repeatedly. The aneurism usually presents close to and lateral to the fornix and upper vaginal wall as a pulsating swelling with a thrill. It may originate spontaneously (Küstner, 36a) or as the result of injury (incision of pericervical abscess (Mundé, Brettauer, 36b), and may burst during labor (Byelicki, 36b) or in the puerperium (Vogelsanger, 36d).

5. **Injuries.**—Of Non-pregnant Uterus.—These are of comparatively infrequent occurrence. Impalement, injury during attempts at inducing abortion (because of suspected pregnancy—Heineck, 37) are uncommon. Operative injuries from brusque dilatation of cervix, introduction of sound or curette through the uterine wall instead of along the sharply flexed canal are of more frequent occurrence (Mayne, 38). The perforation is favored by periods of uterine relaxation and by exceptional softness of the wall (Geyer, Büttner, 39).

The consequences and dangers are more often the result of injuries to neighboring organs (bladder, rectum, intestine, mesentery or omentum) with resulting peritonitis or hemorrhage, than bleeding or infection due to the uterine tear. Peritonitis from irrigation fluid entering the peritoneal cavity, through the rent, is also of frequent occurrence. The injuries vary in shape and extent, depending on the instrument inflicting them. Perforation at the junction of the uterine body and cervix are most common, of the anterior and posterior wall below the fundus next in frequency. Dilators may tear the infravaginal part of the cervix. The rent may be extraperitoneal, extending into the base of the broad ligament.

The injuries may be of different character than those just described. The uterine cavity may be obliterated as the result of a too radical curettage in which all trace of endometrium is removed (Werth, 40).

The writer has seen traumatic stenosis of the cervix with consequent hematometra, in one case resulting from the chronic infection set up by a forgotten piece of cervical gauze retained in situ for two years. In a second case a complete sloughing of the cervix is said to have followed during the convalescence from a laparotomy for ruptured ectopic pregnancy. No history of attempt at inducing abortion or other uterine manipulations could be obtained (40a).

Of the Pregnant Uterus.—*Spontaneous* rupture may result from congenital causes such as malformed, hypoplastic uteri, or pregnancy in an accessory horn (Werth, 40) in all of which the wall fails to or is unable to undergo the hyperplasia necessary to accommodate the growing fetus.

Pregnancy in a diverticulum (Schickele, 41), interstitial pregnancy or a gravid incarcerated uterus, may lead to rupture. Tumors such as carcinoma, sarcoma, penetrating

hydatid mole (Waldo, 42), have had a similar outcome. Andecedent scars resulting from infection, from removal of an adherent placenta, from myomectomy or cesarean section, may rupture at any time during succeeding pregnancies, or weakening of the wall from hyaline or fatty degeneration of the musculature may produce the same effect (Füth, 43).

Trauma arises most commonly as a result of attempted abortion. Such attempts may be self-induced, criminal, or therapeutic. The pregnancy may be extra-uterine (Heineck, 37). The resulting secondary injuries, most often due to carelessness or gross ignorance, are numerous. Omentum, mesentery, loops of gut, have been brought through the rent and torn away (Mayne, 44); perforation of bladder and instestine, a ureter torn out (Wertheim, 45) result; Frankel (45, p. 114) reports avulsion of part of the sacral promontory and intervertebral disk.

The uterus has been injured through the abdominal wall by the horns of cattle (Estor and Puech, 46), stabs and bullet wounds (Robinson, 47), falls, etc. (Robb, 48).

During pregnancy the hemorrhage is a more serious factor than in the non-pregnant womb; infection of the peritoneal cavity, injuries to viscera and puerperal infection make the accident a serious and often fatal one. Yet extrusion of the fetus into the peritoneal cavity with continued growth (Robb, 48) encystment and final development of a lithopedion are on record.

During labor also, spontaneous and traumatic rupture takes place. Small, lateral, bilateral and stellate tears of the infravaginal part of the cervix are physiological.

Spontaneous rupture is predisposed to by the congenital causes mentioned in the previous paragraphs, and by the scars there also mentioned.

Shufflebotham (48a) has operated upon three cases in which the uterus ruptured though the os was undilated and the membranes intact. Frequently repeated pregnancies, and consequent weakening of the muscle appeared at fault.

Mechanical causes producing dystocia such as malpresentations and positions, disproportion between pelvis and fetus, tumors blocking the outlet and atresia of the passages, all favor rupture by obliging the muscle to attempt to overcome undue resistance with consequent thinning out and tearing of the passive lower segment (Bandls' ring).

Violent rupture results when the already overstretched lower uterine segment is torn during operative maneuvers such as version, extraction, application or use of forceps and cranioclasty. The tear may have already begun spontaneously (latent incomplete) and be converted into an overt complete one, by the gentlest and most skillful manipulation.

When tears result they are known as *complete* if they extend into the peritoneal cavity, *incomplete* if no communication between the uterine and peritoneal cavity has been established. In order of frequency anterior, lateral and posterior walls are affected. Cervical tears may extend into the broad ligament, over to the pelvic wall or high up into the fundus. If the uterus is markedly anteflexed (pendulous abdomen) or where the lips of the cervix are incarcerated between pelvic wall and presenting part, transverse tears result. With the cervix out of the pelvis *kolporrhexis* will develop, while transverse presentation favors spiral or oblique tears. The torn edges are irregular and

infiltrated with blood. The uterus may expel the fetus or placenta or both into the peritoneal cavity or broad ligament and contract firmly. Hemorrhage, shock, peritonitis, secondary injuries (ureteral fistula, etc.) are the most common results. A fatal outcome is frequent in the complete variety. Rupture of the uterus intra-partum occurs once in 500 cases. For literature see Lobenstine (49) and Dickinson (50).

II. INFLAMMATIONS

1. **Endometritis.**—Endometritis signifies inflammation of the endometrium, and in these paragraphs is limited to a consideration of the corporeal endometrium. The uterine mucosa, just as other mucous membranes, is subject to acute and chronic inflammations. The acute inflammations are readily recognizable by etiological and histological criteria. Chronic endometritis has given occasion to much error and confusion. The descriptions and classifications before 1907, before Hitschmann and Adler (51) placed the pathology of the disease upon a sound basis, are now mainly of historical interest. Apparently no new classification has been authorized by the American Medical Association since the report of their committee in 1907 (Tucker, Marcy and Clark, 52). This report antedated the newer knowledge and terminology.

Acute Endometritis and Myometritis.—In this condition, not only the mucous membrane but also the musculature or myometrium may take part in the inflammation. The bacterial organisms which alone produce the disease can regularly be demonstrated. Of greatest importance are gonorrheal disease and puerperal septic infections. The non-puerperal uterus, by unclean intra-uterine manipulation, can also be infected, but usually rapidly rids itself of the invaders, although these may continue to cause lesions in the parametrial connective tissue or adnexa. More rarely toxic chemical or thermal agencies are at fault.

The normal uterus contains no bacteria, the vaginal flora being arrested at the external os (Döderlein, 53). According to Bumm, Menge and others, the cervical canal rids itself of introduced pathogenic organisms within a few hours unless injury to the epithelial covering has occurred or discharges, clots, etc., offer a favorable habitat. The same applies to the uterine cavity. Exceptions to this rule are organisms which can flourish on an intact membrane—the gonococcus and diphtheria bacillus.

Acute Non-puerperal Endometritis.—*Gonorrheal.*—As a sequence to cervical infection, frequently not at the onset of the disease, but during a subsequent menstrual period the gonococcus reaches the endometrium. The studies of Wertheim (54), and Bumm (55) have shown that the mucous membrane is swollen, thick and covered with purulent secretion. Cocci occur in discrete patches on the epithelial surface, penetrate between the cells, but are usually arrested by the subepithelial connective tissue, which responds to the irritation by a dense leucocytic infiltration. The cocci do not enter the depths of the glands. The surface epithelium shows metaplasia, often becoming stratified and at times squamous. At times deeper penetration occurs and myometric infiltration results. These obser-

vations were made on both extirpated uteri and particles of curetted mucous membrane.

Länsimaki (56) has recently studied the progress of the inflammation by examination of curetted particles. During the first two weeks neutrophil leucocytes make up the main component of the subepithelial infiltrate; between the fourth and sixth week lymphocytes predominate; after the fifth week plasma cells appear in increasing numbers and remain for months, persising into the chronic stage. No hypertrophic glands or any surface changes were seen. Toward the end of the acute stage (four to five weeks) the glands show a transitory condition of atrophy. Gonococci were not found within the mucosa.

In the early stages the leucocytes pass through the surface epithelium producing a purulent discharge. Considerable infiltration of the uterine musculature was found by Wertheim (l. c., 54).

Commonly the endometrial infection extends to the fallopian tubes, whereupon the syndrome of acute pelveoperitonitis is set up. In this the uterus plays but a secondary part as the endometrial infection may die out after the chronic stage is reached. Reinfection from the cervix or tubes is possible at any time.

Pyogenic (Septic) Endometritis.—In addition to the causative germs, mainly streptococci, staphylococci or colon bacilli, an injury to the mucous membrane is required to permit penetration of the bacteria.

Operative trauma, introduction of a sound, curettage, dilation, stem pessaries, various devices to prevent conception, supply the necessary trauma. Submucous fibroids or corporeal cancers may also be infected. In the senium a low grade of infection leading to pyometra is noted.

The tissue reaction resulting depends on the virulence of the germs. Ordinarily the uterus shows excellent local resistance with rapid subsidence of the process. Infection of the cellular tissues and more rarely, adnexal inflammation may be set up. A more or less severe metritis accompanies the endometrial inflammation, but except in cases of deep or penetrating injuries, phlebitis or peritoneal complications are rarely caused by metritis in the non-pregnant uterus.

The uterine mucous membrane is covered with purulent discharge. Edema, leucocytic infiltration, hemorrhagic areas, desquamation and in severe processes necrosis of the membrane takes place. Granulation tissue forms if the discharge is prevented from draining away (cervical stenosis); if drainage is adequate rapid regeneration takes place.

Application of *caustics* such as zinc chloride may produce scars and superficial sloughs, which can readily be infected and give rise to acute endometritis.

Bleeding from the uterus is seen after phosphorus poisoning. It also occurs in the *acute infectious diseases* (Massin, 57) such as cholera, typhus, typhoid (Lartigau, 58), pneumonia, influenza (Müller, 59),

scarlatina and smallpox. A marked hyperemia of all layers of the uterus is noted and cloudy swelling of the gland epithelium.

Acute Puerperal Endometritis will more properly be considered in detail in connection with the puerperal infections. Postabortum or postpartum the uterine cavity may be invaded (by active introduction, or by growth from the vagina, self infection) by streptococci, staphylococci, colon bacilli, etc., which set up a pyogenic infection. Depending upon the degree of virulence and the capacity for resistance the denuded uterine surface forms a protective leucocyte wall which may or may not be efficient. A pseudomembranous inflammation results. For details and course of the process see Puerperal Infection, p. 481.

Saprophytic, usually anaërobic, bacteria may cause infection by multiplying on the clots, membranes or retained portions of placenta. The process is superficial, absorption of the bacterial products taking place more often than invasion.

Diphtheria has very frequently been noted (Bumm, 60). The invasion extends by continuity upward from the vulva.

Actinomycosis is usually incidental to pelvic actinomycosis and involves the uterine wall (Marchand, 60a).

2. **Acute Metritis.**—In most cases of puerperal endometritis the succulent and involuting musculature, traversed by large and often thrombosed vessels takes part in the inflammatory reaction (Fig. 128). In severe infections, localized necrosis of part of the wall may occur. A sequestrum results and is cast off within two to three weeks (*metritis dissecans*, Fromme, 61). Breaking down of the tissue may produce *intramural abscess* (Lit. Barrows, 62).

Intramural abscess occurs both in the puerperal and non-puerperal state (1: 1). Often after normal labor stormy symptoms develop in from 2 to 6 weeks. Apparently most cases remain undiagnosed, either rupturing into the uterus or being absorbed. Literature of the condition is scant; Mercadé reported 41, Noble had 8 cases of his own, Sampson 4, and Barrows 7 (62). The latter found in an acute case a pure gonococcal abscess, and in a healed case a calcified body the size of a golf ball, as residuum of an abscess.

Direct extension into the peritoneum may set up a localized or diffuse peritonitis. If the endometrial inflammation subsides, the myometrial infection may do likewise. Increased connective tissue, scars and perimetric adhesions remain as permanent residua.

3. **Pyometra.**—The accumulation of pus in the uterus requires infection and interference with drainage. The commonest cause is cancer of the cervix, which blocks the canal and undergoes infection. (See Fig. 199, p. 278.) (Cullen, 63.) After stenosis of the cervix from repeated cauterization in gonorrheal infections, after removal of submucous fibroids, a purulent collection may accumulate in the uterine body. After opening a hematocolpos and hematometra, ascending infection may be followed by pyometra (Oldfield, 64). Senile pyometra is not infrequent. The atrophy

of the uterus and shrinking of cervix and vault produce stenosis, the flaccid corpus does not expel its contents and small accumulations form without producing disturbance except purulent discharge. In cases of tuberculosis of the uterus, tubercular pyometra is seen (Oldfield, l. c. 64; Kaufmann, l. c. 2: 1009). Physometra may develop if gas-producing organisms penetrate secondarily.

The pus in pyometra may be sterile; it may contain colon bacilli or saprophytes. The collection of pus may spontaneously evacuate through the cervix, may also cause gangrene of the uterine wall, rupturing into peritoneal cavity, parametrium, bladder or rectum. In carcinoma of the cervix the pyometra is of importance because it may

FIG. 128.—ACUTE METRITIS. (L.P.) (Edema of uterus due to pelvic inflammation.) Section taken close to peritoneal surface of a large edematous uterus. The edema has crowded the bundles of muscle fibers widely apart. 1. Capillary vessels. 2. Bundle of muscle fibers. 3. Edematous connective tissues.

unfavorably affect the postoperative course by causing infection of the wound or peritoneum.

Histologically, depending upon the severity of the infection, the duration of the process and the amount of pressure exerted by the fluid, the mucous membrane is found densely infiltrated with leucocytes, surface epithelium lacking in spots, gland epithelium poorly staining, in mild and early cases. In severe infections the mucosa is changed into a pyogenic membrane (Fig. 129). After drainage is established, the degree of restitution possible (except in carcinoma and tuberculosis) depends upon the amount of preceding destruction. In severe grades complete obliteration of the corporeal cavity may result.

Epidermoidalization of Endometrium *(Psoriasis uteri)*.—This very rare condition may be noted on the surface of uterine polyps, in pyometra (Bondi, 65), and in gonorrhcal endometritis (Wertheim, 54), Menge, 66). Of broad extent and in spots showing down growth, a case was reported by v. Rosthorn (67). More or less extensive islands of squamous-celled epithelium, sometimes with cornification, replace areas of normal surface epithelium. Regularity of cell distribution, absence of small round-celled infiltration zone and presence of prickle cells distinguish these changes from carcinoma.

Metaplasia of the cylindrical epithelium, as happens in response to various stimuli (inversion, etc.) accounts for the phenomenon.

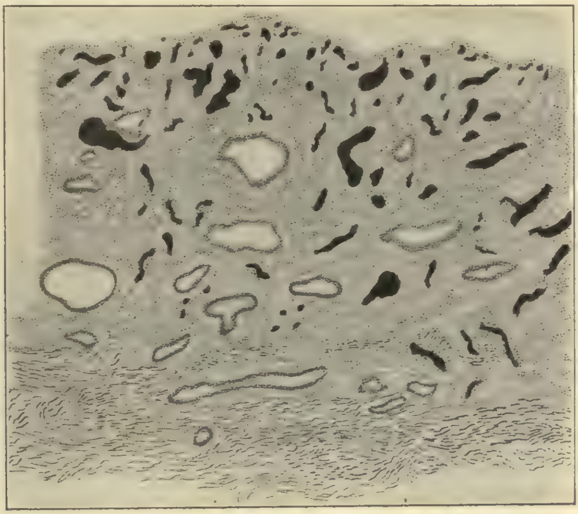

Fig. 129.—Pyometra in a woman of 64 years. (L.P.) The superficial layers of the endometrium are converted into a pyogenic membrane (leucocytes, new-formed blood vessels). Intermediate layers are heavily infiltrated with leucocytes, yet glands remain intact though with poorly staining epithelium. The deepest layer and musculature are almost normal.

Hofbauer (68) found the cervical canal lined with plaques, as if pieces of skin had been transplanted.

The frequency with which this condition was noted by Zeller (69) was apparently due to the fact that he regarded fragments of vaginal epithelium accidentally mixed with curettings (Fig. 235, p. 370) as evidence of epidermoidalization.

4. **Chronic Endometritis.**—Chronic endometritis is difficult to recognize because the usual criteria of chronic inflammation, exudation, vascular changes and stroma reaction, which manifest themselves as edema, hyperemia, round- and plasma-cell infiltration and perhaps gland hyperplasia —even if present, may be obscured by almost similar phenomena which

periodically occur in response to the menstrual cycle (see Chapter IV, p. 76). The cyclical changes may, moreover, be excessive, in response to excessive ovarian stimuli, and quite independent of inflammatory excitation (Stationary hyperplasia, p. 194).

In Chapter IV, the glandular, interstitial and vascular cyclical changes were described in detail. A brief review of the most salient features to be kept in mind will, however, be of use.

The interval is marked by resting, on cross section circular glands, widely separated by cytogenic stroma. This period lasts approximately 18 days.

The premenstrual or secretory stage shows a greatly thickened mucosa with three distinguishable layers—(1) a surface layer with narrow gland mouths and very decidual stroma; (2) a broad middle zone containing the close-set, convoluted, diffusely staining glands characteristic of this portion of the cycle, the stroma less markedly decidual and (3) a narrow, basal layer with unchanged gland fundi and barely changed stroma. This stage lasts from 6 to 7 days.

Menstruation is distinguished by increasing capillary hyperemia, by edema, and finally by extrusion of red blood cells into the stroma and lumen of the uterus. Schroeder describes complete destruction of the superficial layers.

Until the new era began in 1907, interval mucosae were catalogued as "chronic interstitial endometritis," premenstrual changes as "chronic glandular and hyperplastic endometritis," and bleeding mucous membranes as "hemorrhagic endometritis," quite irrespective of either clinical or histological criteria.

Hitschmann and Adler (l. c., 51) concluded that interstitial endometritis is the sole chronic form that can be demonstrated, but that non-inflammatory glandular hyperplasia (Frank, 70) does occur. It is no longer deemed necessary to review in detail the enormous number of articles which were published between 1907 and 1913 agreeing with, modifying or attempting to controvert the original investigation. The salient facts are generally accepted. The literature is reviewed in the articles of Gardiner and Novak (71), Norris and Keene (72), Albrecht and Logothetopulos (73), Frank (70), Strong (74), etc., etc. The main questions still somewhat at issue are:

1. The degree of variation from cyclical changes to be still considered physiological.
2. What criteria pathognomonic of inflammation elsewhere in the organism are recognizable in the endometrium.
3. To what extent to limit the concept of chronic endometritis as a clinical and pathological entity.

1. The degree of variation from cyclical changes to be considered physiological. Büttner (75) emphasized the finding of hypertrophic, poorly involuted glands in the postmenstruum or early interval—*lack of*

correspondence with the phase. Mixture of phases, that is, pictures characteristic of two or all of the phases in the same specimen were reported by Hartje (76), Hegar (77). This, according to Albrecht (78) and Strong (74), is an artefact due to curettage in which the unchanged basal layer is mixed with the more superficial layers. In the writer's opinion this explanation will not apply to all cases.

So-called "invagination" of glands (Fig. 130) is likewise called an artefact, due to shrinkage of curetted specimens, Albrecht and Logothetopulos, 73; Watson, 79). The writer agrees with Frankl (l. c. 45, p. 27) that these pictures may occur in extirpated uteri as well. They merely signify gland activity.

FIG. 130.—INVAGINATION OF GLANDS. (M.P.) The endometrium is in the resting stage showing artefacts which produce concentric rings of epithelium in the gland lumen. 1. Projection of epithelium into gland, pedicle intact. 2. Section below pedicle resulting in two circles of epithelium. 3. Three epithelial circles. Explanation of this is shown outside, on the margin of the circle. (A) Longitudinal section of gland with invagination at its base. (B) Cross section of same gland through region of broken line in (A). 4. Oblique section of gland produces areas of pavement epithelium at each end.

Complete independence of phase, that is, permanent hyperplasia, has been emphasized by Albrecht (78). But, contrary to Albrecht's views, cyclical changes may be superimposed upon the permanently hyperplastic mucosa (Fig. 138, p. 195).

None of the above are strictly physiological, none of them, however, have been found to be due to inflammatory reactions. Most of them can be ascribed to prolonged or excessive ovarian stimulus.

2. What criteria of inflammation elsewhere in the organism are recognizable in the endometrium?

Experience and subjective opinion must doubtless continue to play a rôle, but too great a latitude should not be permitted. The presence of plasma cells in great number are a sure sign of inflammation. They appear in only a moderate percentage of cases—37.5 per cent (see footnote 11, Frank, l. c. 70), and may disappear within a few months, as has been shown especially by Länsimaki (56) in gonorrheal endometritis. Some observers fail to find any (Voigt, 80), others report them in 50 per cent of specimens examined (Freund, 81; Weisshaupt, 82).

Hyperplasia of glands is regarded by some observers as an indication of inflammation (Albrecht, l. c. 78); by the majority, including the writer, it is claimed that if occasionally of inflammatory origin or accompanying inflammation, no proof of its regular occurrence in this connection has been offered (Büttner, Theilhaber and Meier, Schroeder, 83). It is therefore useless as a criterion.

Leucocytic and round celled infiltration (Albrecht, l. c. 78), vascular changes including increase in number of capillaries and thickening of their walls (Keller, 84), presence of mitoses in early interval (Büttner, 75) have been shown respectively to disappear early, to be due to the cycle, or to be subject to individual interpretation.

The writer is free to confess that he is unable to recognize "scars," perivascular infiltration, or obliteration of the three premenstrual layers, especially in curetted material.

3. To what extent should the concept of "chronic endometritis" be limited? Should this concept be based on clinical conditions, or on pathological criteria?

A clinician should recognize that a majority of patients who complain of the conventional symptoms of "endometritis" (leucorrhea, pain, bleeding, and backache, etc.), show no corresponding pathological changes in the uterus. Leucorrhea is usually of cervical origin; bleeding is due to ovarian or other cause (p. 177). Moreover, many cases which show anatomical evidence of inflammation show no corresponding clinical symptoms. Bacteriologically, these uteri are sterile (Curtis, 85; Henkel, 85). Exaggeration of the cyclical change and hyperplasia occur independent of inflammation. This includes polypoid and cystic endometria.

Therefore the clinician will be obliged to reclassify the symptom complex known as "chronic endometritis" and distribute it among ovarian functional conditions, diseased adnexa, postpartum subinvolution, etc., where they belong.

The pathologist can recognize chronic endometritis when plasma cells are present. This requires special fixation and special stains. Even if clear evidence of myometritis persist in removed uteri, the mucosa may already have purged itself of the invader. The writer is unable to recognize round-celled infiltration in the chronic stage or scars, in the endometrium. From the literature it would appear that others have developed greater diagnostic acuity. Lack of correspondence in phase, especially premenstrual changes,

as distinguished from stationary hyperplasia (p. 194), must be ascribed to ovarian influences. Stasis, for example, does not produce it as Büttner (l. c., 75) has shown in retroflexed and prolapsed uteri. Cystic endometrium such as is seen at puberty and preclimacterium, stationary hyperplasia, and bleeding uteri (Figs. 131 and 132), show no signs of inflammation, unless inflammation is superimposed upon the original process, a most infrequent coincidence.

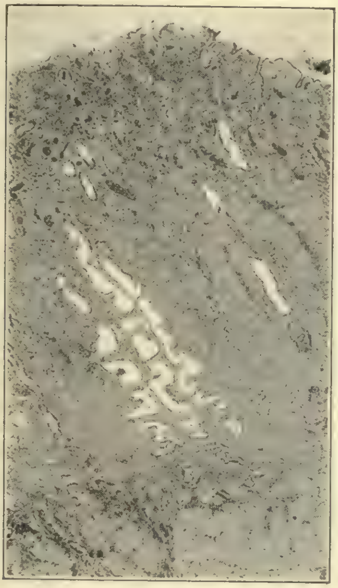

FIG. 131.

FIG. 132.

FIG. 131.—NORMAL MENSTRUATING UTERINE MUCOSA. Photomicrograph. (L.P.) Toward lumen, slight loss of surface epithelium. Superficial layers markedly infiltrated with blood, sufficient to destroy glands. Deeper layers show corkscrew glands, moderate amount of blood corpuscle. Deepest layer close to muscle unchanged.

FIG. 132.—MUCOSA OF UTERUS, REMOVED FOR CONTINUOUS BLEEDING. Photomicrograph. (L.P.) (During one year three curettages.) Note that the mucosa cannot be distinguished from normal as seen at the beginning of menstruation.

Chronic endometritis, therefore, as has been shown, is an uncommon disease, because the uterus is an unusually well drained organ, and because the cyclical changes with the resulting hyperemia and deturgescence are unfavorable to the continuance of the growth of most microörganisms. When present, the disease appears to play no clinical rôle, being overshadowed by the accompanying lesions—endocervicitis, salpingitis, etc. Heretofore it has most often been confused by the pathologist with endometrial hyperplasias due to ovarian overfunction, or, by the clinician, with uterine hemorrhages (with normal endometrium) resulting from the same cause. Doubtless in some of these conditions a chronic inflammation (recognizable or occult) may also be present. However it would appear

that the endometritis is merely incidental and plays no distinctive rôle. The chronic myometrial changes will require separate discussion.

In order to reduce the disturbing influence of the cyclical changes to a minimum, clinicians are advised, whenever possible, to curet the uterus shortly after menstruation has taken place. Premenstrual changes are thus excluded.

5. **Chronic Myometritis.**—After excluding the "hyperplastic myometrial conditions" (p. 194), enlargement consequent to fibroids (p. 242), and the cases of true subinvolution (p. 196), very few remain to be considered in the category of true chronic inflammations. Acute metritis may become chronic if persistent and recurrent gonorrheal infections with foci in the cervix and adnexa keep the process alive. The same applies to puer-

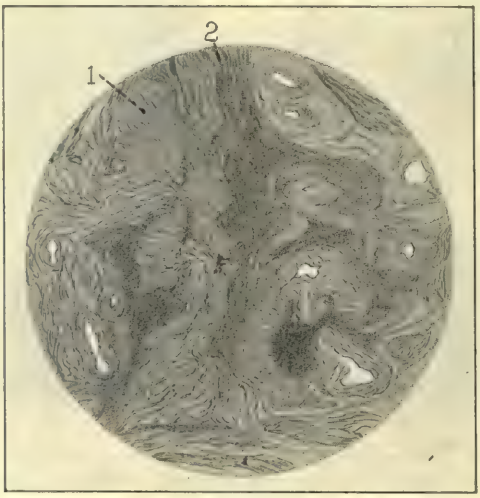

FIG. 133.—SUBACUTE METRITIS. (L.P.) In many areas the muscle bundles of the uterus are infiltrated and crowded apart by a dense round-cell infiltrate. In some areas the neighborhood of the vessels is free, in others it is most densely infiltrated. 1. Muscle bundles. 2. Area of round-cell infiltration.

peral infections in which adnexal trouble also continues to fan the inflammatory reaction, and is assisted by continued cervical reinfection (from lacerations and ectropion). Perimetric processes and exacerbations of pelveoperitonitis keep up the vicious circle. The endometrium may or may not be involved.

The uterus is enlarged thick, boggy, in the earlier stages; hard and enlarged later in the process, and may finally show atrophy in the latest fibrotic stage (Kaufmann, l. c. 20 b, 2:1010).

Histologically, increase in connective tissue, round-celled infiltration in the septa and along the blood vessels during the earlier stages and during exacerbations (Fig. 133), and true scar formation in the healed condition are noted.

6. **Dysmenorrhea Membranacea.**—The disease is characterized in most typical cases by the periodic expulsion at each menstrual period of complete casts of the entire uterine cavity, accompanied by extreme cramp-like pain. Variations, which include the occasional expulsion of small fragments or fibrinous looking clots with mere discomfort or no pain, mark the other extreme.

The disease may appear at puberty, or later in life. It is most often found in sterile women (Löhlein (86) of 27, only 6 not sterile), though it has begun or continued after childbirth. The writer has seen it in patients coincidentally suffering from membranous colitis. Löhlein (l. c. 86), Mayer (87) have observed it in mother and daughter. No definite etiology has been found, since an inflammatory basis has been disproved by Hitschmann and Adler (88), and Ascheim (89) found the endometrium bacteriologically sterile. Halban (90) regards ovarian overfunction as the cause. The condition appears due to premature uterine contractions which produce separation of the functional layers early and *en masse.*

Grossly, the complete membrane, if such should be passed, an uncommon finding, is identical in appearance with the "casts" of extra-uterine pregnancy (see p. 447). A three-cornered, shaggy sac, with two small openings at the lateral angles and a larger hole at its apex, the inner surface smooth (occasionally showing pinpoint openings of glands), thickness from 1 to 3 mm., color whitish gray to dusky red or completely blood-infiltrated and clotlike, describe its appearance. The membrane may consist of small fragments of the above or of apparently plain lamellated thin sheets of blood clot.

Microscopically, two main types are encountered (Kollmann, 91). In the more *common* type a more or less complete cast of the superficial layers of the endometrium is formed. The decidual stroma reaction is well marked, the gland outlets appear, but the lining epithelium may be absent or macerated. Considerable thickening or hyaline changes in the vessel walls are of usual occurrence. Round-cell infiltration is widespread (Fig. 134). In the other type, red blood cells, round cells and leucocytes appear embedded in a fibrinous network which here and there gives a suggestion of the outline of former glands (Fig. 135). The writer in the numerous specimens which he has examined, has never seen any corresponding to the membranes consisting of polygonal pavement epithelium described by Beigel (92).

Diagnosis.—It is important to differentiate between early abortion (Fig. 136), cases of extra-uterine pregnancy, and dysmenorrhoic membrane. The degree of decidual change of the stroma cells may be alike in all three. Chorionic villi are decisive for abortion. The criteria proposed by Abel (93), absence of uterine glands and an endothelial-like surface epithelium in ectopic pregnancy, are not reliable or constant. Nor is Blair Bell's (94) assertion that "microscopically, however, it is quite a simple matter for anyone accustomed to examine these specimens to distinguish between the two," borne out by the testimony of some of the best known microscopists.

His criteria are poorer preservation of the decidual cells, smaller size and wider separation of the cells in menstrual membranes. The appearance may coincide so closely as to defy diagnosis by the microscope.

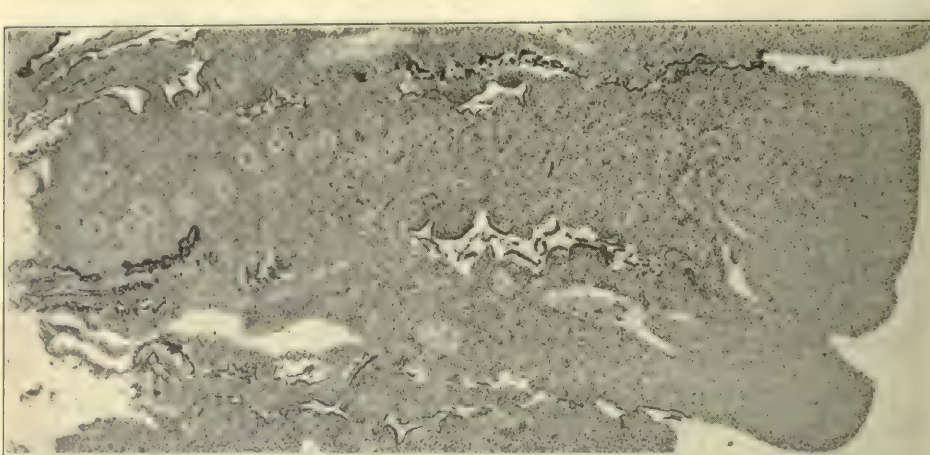

FIG. 134.—PHOTOMICROGRAPH OF DYSMENORRHOIC MEMBRANE. (L.P.) The membrane consists of two layers. The outer one is composed of a dense mass of decidual cells (compact layer), the deeper layer contains irregular glands with desquamating epithelium and numerous cross sections of blood vessels with hyaline degeneration of their outer coat. (Spongy layer.)

FIG. 135.—UTERINE CASTS. (L.P.) Expelled by a young woman who had been bleeding for three and one half months. No structure determinable. Cast consists of a fibrin network infiltrated with leucocytes. No diagnosis possible.

Dysmenorrhea or painful menstruation unaccompanied by an exfoliative membrane is a common affection. Attempts to demonstrate an anatomical basis are but partly successful.

Primary hypoplasia, appearing as underdeveloped uterus, cochleate uterus, or uterus with long conical cervix with pin-point os, most often is present in dysmenorrhea. Yet the pain may not develop until long after puberty has set in, may be relieved by such diverse measures as dilatation of the cervix, or plastic operation on the cervical canal, regular sexual relations, cauterization of the "genital" spots of the nose (Fliess, Mayer, Brettauer, 95), or childbirth. Bell (96) believes the pain due to "blocking

FIG. 136.—CURETTING POSTABORTUM: SUBINVOLUTION, MARKED BY BLEEDING. (L.P.) The central part is composed of a poorly preserved stroma infiltrated with round cells and containing a few glands. 1. Uterine gland. 2. Decidual cells. 3. Large area of decidual cells surrounding blood vessels. 4. One of several small arteries showing decidual change of vessel wall and surrounded by scattered decidual cells. 5. Fairly normal endometrium. (Stroma and glands.)

of waves of contraction." His anatomical pictures representing the irregular development and fibrosis of the musculature are far from convincing.

Dysmenorrhea often, but not always, accompanies inflammatory diseases of the adnexa. It may be found in gross mechanical obstructions such as uterine polypi, or submucous fibroids, or where the menstrual blood is expelled in clots.

Why the menstrual blood fails to coagulate has given rise to much controversy. Christea and Denk (97) believe the endometrium holds back or inhibits the fibrin ferment (dialytic theory); Sturmdorf (98), Schickele (99) that an inhibiting element is produced by the endometrium. Blair Bell (100) describes real blood casts which produce pain during expulsion, Kaufmann (l .c. 2: 997) similar clots with projections extending into the tubes. The contradictory results obtained require further confirmation and elaboration before serious consideration can be accorded them.

Vicarious menstruation has never been elucidated, nor has an anatomical substrat been demonstrated. It may occur instead of uterine bleeding in congenital aplasia, functional amenorrhea, or in addition to the uterine bleeding. Bleeding from the nipple, nose bleeds, hemoptysis, and hematuria have been reported in decreasing order of frequency. For literature see Schaeffer (101).

7. **Hyperplastic Conditions.**—1. STATIONARY HYPERPLASIAS *(Including polypoid and cystic endometria).*—Irrespective of the menstrual phase a thick (1 to 1.5 cm.), nodular or polypoid endometrium, usually pale yellow and often semi-transparent, may be found in certain cases of persistent uterine hemorrhage. Often the endometrium is also cystic. Not infrequently diffuse thickening of the myometrium or fibromyomata (in 50 per cent according to Schickele and Keller, 102) coincidentally occur. The mass of curettings obtained far exceed that from a normal premenstrual stage.

The *histological picture* is that of a very thick, often edematous mucosa, in which the glands may or may not show the proper cyclical changes (Figs. 137 and 138). Mitoses are frequent even in the early interval (38 per cent, Albrecht and Logothetopulos, l. c., 73). Albrecht (78) and Hartje (76) emphasize the absence of the three layers repeatedly referred to. The writer has not found this rule invariable. No other distinguishing marks appear characteristic, although various authors have so regarded grouped vessels with thick walls (Henkel, 85); epithelium sharply defined against the lumen (Frankl, l. c. p. 28); true intraglandular papillae (in contradistinction to pseudo-papillae, see Fig. 72, p. 84), Hartje (76), etc. Signs of inflammation are absent in the great majority of instances.

In severe hemorrhages at the onset of puberty, and even more regularly in the hemorrhages of the preclimacterium, cystic gland changes may predominate in these hyperplastic mucosae (Fig. 139).

The above conditions appear due to continued and excessive ovarian stimuli, which Hartje unsuspectingly but graphically described as "subinvolutio deciduae menstrualis," and are frequently associated with the group of cases next to be described.

8. **Hyperplasia of the Myometrium** (FIBROSIS UTERI).—Under this name are included a group of cases variously called "chronic metritis," "fibrosis uteri," "arteriosclerosis uteri," "metrorrhagia myopathica," etc. A large, hard uterus measuring from 4 to 4½ inches in length, with a wall

double the normal in thickness, resistant to the knife, showing fibrous strands and projecting blood vessels on the surface of the gross section, characterizes this disease. The endometrium may or may not be hypertrophic. The patients are usually toward the end of their sexual life. Before the use of X-ray or radium was known, the writer was obliged to perform hysterectomy on a woman of 21 years to prevent loss of life from hemorrhage.

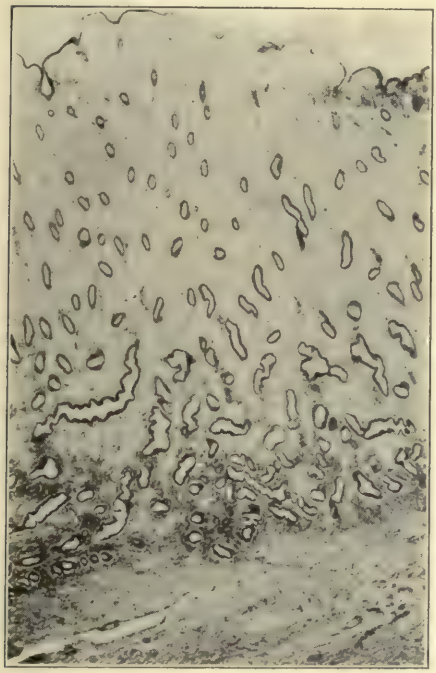

FIG. 137.

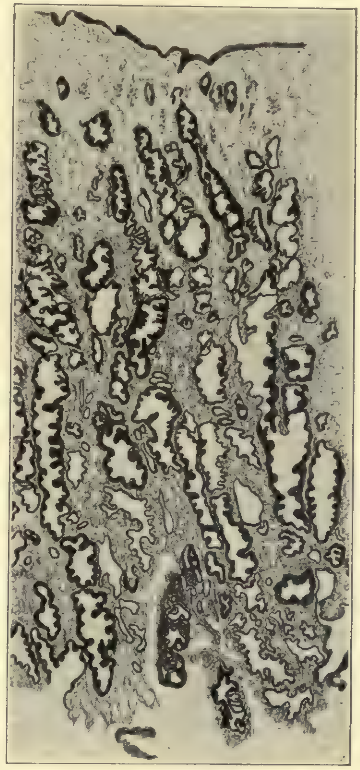

FIG. 138.

FIG. 137.—PHOTOMICROGRAPH—EDEMATOUS HYPERTROPHIC UTERINE MUCOSA. (In the early interval.) As seen in "polyposis uteri" and in fibroids (where free from pressure). Endometrium is from 9–10 mm. thick. Glands separated by edema which does not affect the deepest layer.

FIG. 138.—SO-CALLED STATIONARY HYPERPLASIA OF UTERINE MUCOSA. (L.P.) The thickened mucosa in this instance shows the premenstrual glandular and stroma changes but remains permanently hypertrophic even during the period of rest. This condition is regularly seen in fibroid uteri and uteri with polypoid endometrium, probably caused by continual overstimulation from the ovary.

The causes supposed to produce this condition are so numerous and have so regularly failed to withstand critical inquiry, that the writer is convinced that none of them are truly etiological.

Reinicke (103) considered arteriosclerosis of the large vessels the main

factor, disproved by Pankow (104); Theilhaber (105) found an excess of fibrous tissue at the expense of the musculature (contraverted by most exact measurements of Schickele and Keller (106); Findley reported a combination of the two (107); Anspach (108) regarded lack of elastic tissues in the vessels and in the mesometrium important; and Goodall (109) and also Shaw (110) believe that the increased accumulation of elastic tissue around vessels, which they characterize as the main sign of subinvolution, is

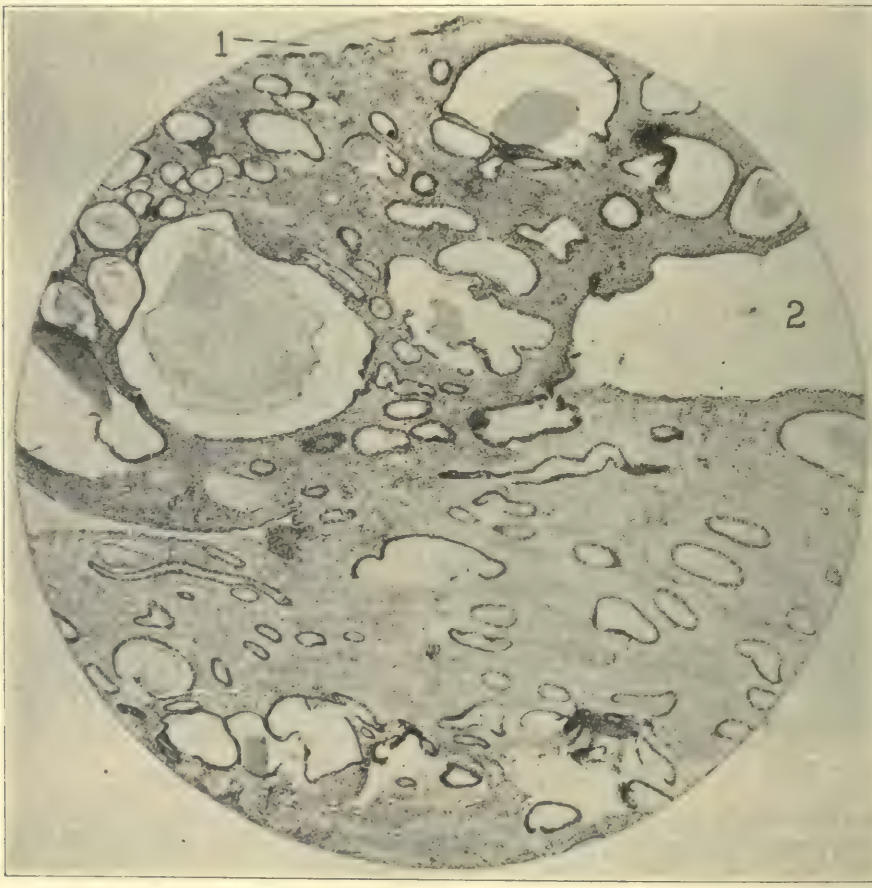

FIG. 139.—PHOTOMICROGRAPH—POLYPOID AND CYSTIC CHANGE IN THE ENDOMETRIUM. ("Endometritis fungosa of Ohlshausen"). Change seen most often with puberty and preclimacteric hemorrhage. 1. Surface epithelium lining uterine cavity. 2. Dilated gland.

the chief cause of the hemorrhage. Shaw (110) reports one hundred cases of which he classifies 95 as subinvolution, 4 as hypertrophy (in which the endometrium is 1 to 1.5 cm. thick) and one as true chronic metritis as evidenced by the perimetric adhesions. For literature consult Hirsch (111), Shaw (l. c. (110)). The utmost unanimity exists as to the absence of evidence of inflammation.

The writer agrees with Frankl (p. 26) that in the earlier stages muscular, in the later stages fibrous tissue predominates in forming the bulk of the thickened uterine wall.

He is also in accord with Schickele and Keller, who state that the bleeding is due to ovarian influences. Moreover, in substantiation of this opinion, he offers the proof of immediate and great hyperplasia of musculature and endometrium obtainable in animals upon injection of corpus luteum extracts (Fig. 140). Whether long-continued exhibition of the extract will produce fibrotic changes remains to be tried. The fact that X-ray exposure of the ovary regularly cures the bleeding is additional proof of an ovarian origin of the disease.

FIG. 140.—PHOTOMICROGRAPH OF RABBITS' UTERI. (L.P.) To show effect of injection of placental extracts. 3 and 4. Before and after injection of alc. sol. extract, daily injection for 11 days.

9. **Atrophy of Endometrium and Myometrium.**—Primary hypoplasias are considered in connection with malformations (p. 497). Atrophy implies regression.

It may be purely *functional,* as seen during lactation, but if excessive and permanent, becomes pathological (Thorn, 112). Any cause which produces ovarian hypofunction induces uterine atrophy. The extreme degree is seen after double oöphorectomy, precocious climacteric (Stark, 113) to a less extent following X-ray exposure of the ovaries; the minor degrees are noted in the course of debilitating diseases—chlorosis, tuberculosis, etc.—and in certain stages of endocrine disturbances, thyroid, pituitary, see p. 507), rarely as sequel of infectious diseases such as typhoid (Gottschalk, 114), or in chronic poisoning such as morphine habit (Olshausen, 115). In a broad sense the causes of amenorrhea and atrophy overlap or coincide.

Atrophy may also result from *traumatic and inflammatory causes.* Excessively deep curettage, protracted atmokausis, too radical cauterization with chemicals may permanently destroy the endometrial mucosa. Similarly, destructive processes may develop as the end result of puerperal infections and of pyometra. Pressure as seen in submucous fibroids may cause endometrial atrophy at the most prominent pole of the tumor (Fig. 164) or pressure by pelvic tumors may cause concentric atrophy of the entire organ.

In the functional atrophies, both muscle and mucous membrane diminish in thickness and succulence. If permanent, fibrous tissue to a great extent replaces the musculature. The organ approaches the condition of senile atrophy (p. 38), and in extreme cases may shrink to minute proportions.

If cavity and general size of the uterus diminish in proportion, the atrophy is called *concentric.* If the cavity fails to diminish, the change is known as *excentric.* The cervix may or may not partake in the general atrophy.

10. **Endocervicitis.**—The cervical mucous membrane does not undergo cyclical changes, takes part only to a minor degree in the changes of pregnancy, and is well shut off from the uterine cavity. Consequently the cervical and corporeal cavities enjoy considerable independence of each other. Leucorrheal discharge is mainly of cervical origin.

The inflamed cervical mucous membrane becomes swollen and edematous. A great increase in secretion takes place. This may be purely mucoid or mucopurulent or tinged with blood. Dense infiltration of the interglandular stroma with leucocytes, is the main lesion in acute inflammations. As the subacute and chronic stage is reached an increasing number of

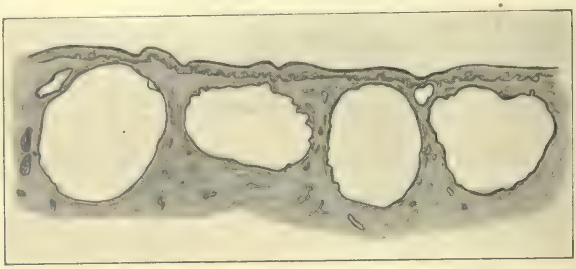

Fig. 141.—Nabothian follicles in the cervix. (Very low power.) Dilatation of closed off glands produces thinning of epithelial lining, distention of lumen with consequent cyst formation, and flattening out of rugae. On extreme left a few as yet, undilated glands with normal columnar epithelium are shown.

plasma cells are encountered. The glands increase in size. Their outlets are often obstructed and retention cysts (nabothian follicles) result. These cystic structures whose lining epithelium has become low cuboidal from pressure, may honeycomb the cervic in every direction, increasing the infravaginal portion to large dimensions and presenting grossly the picture of a tumor (Fig. 141).

Gonorrheal endocervicitis commonly halts at least for a time, at the internal os—but particularly during menstruation, it may extend into the corpus. The great extent and rugosity of the cervical mucosa affords innumerable safe hiding places to the gonococcus. To puerperal septic infection the lacerated and bruised cervix affords ready access. Infections of both the mucous membrane and stroma of varying degree occur. Necrosis and sloughing may produce stenosis of the canal.

Hyperplasias due to ovarian influences do not affect the cervix. Slight changes result from changes in blood supply to the entire uterus. The cervix takes part in atrophies.

11. **Cervical Erosion: Ectropion.**—As a result of cervical inflammation, especially after it has reached a chronic stage, bright red, often elevated

areas are seen around the circumference of the external os. These areas usually become continuous with the mucosa lining the cervical canal, but may form discrete patches. Still more rarely the entire portio vaginalis up to the fornices is affected by the process, appearing brilliant red, hypervascular and covered with discharge. The feel is soft and velvety or granular. Bleeding results upon the slightest touch. Because of cursory resemblance to carcinoma, tuberculosis and syphilis excised specimens are often sent to the pathologist for diagnosis.

The etiology of the condition has given rise to much research and speculation. Its histology is clear.

The earliest stages, according to R. Meyer, Schottländer (116) and others, is represented by an infiltrated area denuded of squamous epithelium, due to necrosis and maceration of the surface layer. The papillary layer of the cervix is densely infiltrated by round cells. Cervical glands growing downward from within the cervical canal (Münzberger, 117)

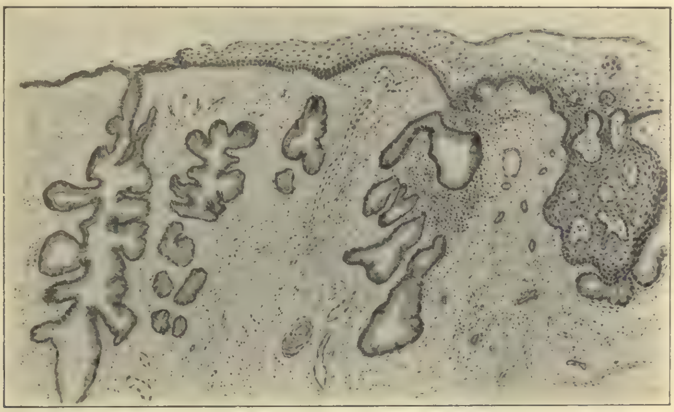

FIG. 142.—CERVICAL EROSION. (M.P.) To left, columnar epithelium (eroded area), on right, squamous epithelium creeping in. On right, gland filled by squamous epithelium. In middle, numerous cervical glands surrounded by infiltrated stroma.

approach the denuded area from below. This is the stage of true erosion consisting of superficial ulceration, granulation tissue and gland invasion. It is of short duration and rarely seen.

In the *early stages of healing* the bright red area is covered by high columnar epithelium with oval, basal nucleus. The cells stain with mucicarmin, like true cervical glands. Below the surface are more or less numerous branched glands. The stroma is densely infiltrated. The picture is that of an inflamed portion of the cervical canal bodily transplanted to the portio (Fig. 142). If the surface is smooth, the glands few in number and not dilated, the erosion is *simple;* if the glands are numerous and dilated, lined by high, narrow epithelium often assuming pseudo-papillary forms and containing goblet cells, *a follicular erosion* is said to exist, its surface being granular; if the glands are numerous, run downward parallel to each

other, a *papillary* appearance is presented (Fig. 143) because of the numerous stroma papillae which project upward between the glands.

In the later stages of healing, as the inflammation subsides, squamous epithelium grows in from the sides, or regenerates from islets still remaining

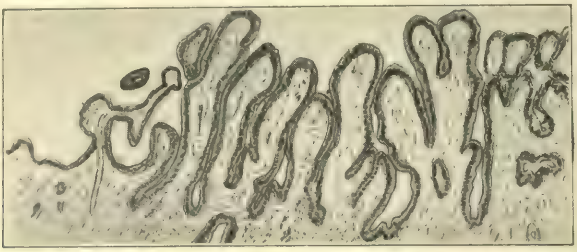

Fig. 143.—"Congenital erosions." (M.P.) Showing markedly papillated surface. The folding of the surface produces the velvety appearance seen both in congenital and papillary erosion.

here and there, growing beneath the columnar epithelium and displacing it (Fig. 144). The squamous epithelium enters the neck of glands, in some cases succeeds in entirely replacing the cervical variety, filling the gland with a solid squamous plug (Fig. 145). In other cases the gland mouths are

Fig. 144.—Healing erosion. (M.P.) The columnar epithelium on the surface has been completely substituted by squamous epithelium which is "creeping into the opening of glands." Eventually the glands will be filled with squamous plugs. As a final stage of healing flattening out of these plugs will occur.

closed off and retention cysts (nabothian follicles) result. Relapses are frequent, in which part of the squamous epithelium is again desquamated and replaced by the cervical variety.

The final healing takes place when the cervical glands have been converted into solid epithelial plugs which eventually flatten out into the general surface covering (Fig. 142, right edge).

The increase in size and number of glands may produce localized or diffuse tumor-like hypertrophies with irregular tonsil-like surface (Schroeder, 118), which may reach large size and resemble adenoma.

The theories devised to explain the etiology of erosion are many. None are completely satisfactory.

Embryonal.—Fischel (119) showed that in 36 per cent of newborn, the portio is covered with a single layer of cylindrical epithelium with frequent persistence of cervical glands (congenital erosion). In later life if the replacing squamous epithelium desquamates, the epithelium from persistent fetal glands covers the denuded surface with a cylindrical layer.

Eversion.—Roser, Emmet (120) and others regard the erosion as an eversion of the normal cervical epithelium due to cervical laceration or to protrusion through the uninjured os externum in consequence of edema and

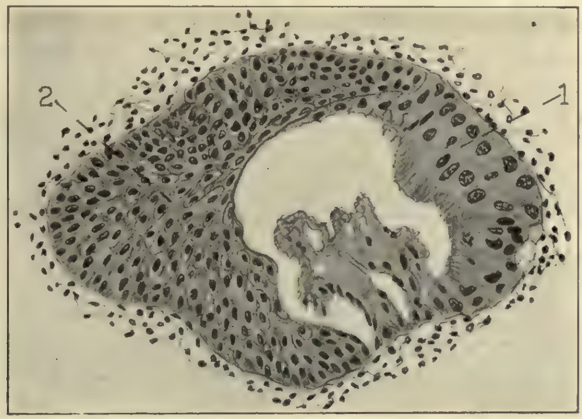

Fig. 145.—Transverse section of cervical gland. (H.P.) From Fig. 144, near junction of squamous and columnar gland epithelium. 1. Cervical epithelium. High columnar. 2. Squamous surface epithelium growing down from surface. This picture shows a slight resemblance to carcinoma. Malignancy is excluded by the uniform size and regular distribution of the squamous cells.

swelling. Exposed to the acid vaginal discharge and the friction of the vaginal walls secondary metaplastic changes develop.

Inflammatory.—Ruge and Veit (121) regarded the cylindrical epithelium as a metaplastic change arising from the basal germinative prickle-cell layer normally covering the portio, after all the superficial layers have been cast off by maceration. Downgrowth of these germinative cells then form the erosion glands. Schottländer (116) amplifying Münzberger's theory, regards the glands as derived from cervical glands growing downward into the portiovaginalis under the stimulus of the inflammatory irritation. Arrived below the squamous epithelium of the portio they break through and eventually replace it. R. Meyer (116) has the simplest explanation, considering the first stage a simple denudation, i.e., ulcer, the

cervical epithelium growing in from the edges to cover the denuded area (Figs. 146 and 147). For detailed description see Adair (122).

FIG. 146.—HEALING ULCER OF CERVIX. (Very low power). The denuded area in the center is covered with granulation tissue and exudate. The squamous epithelium is creeping in from each side. The small square indicates area drawn in higher magnification in Fig. 147.

The extremely varied configuration presented by intermingling of the two types of epithelium upon the surface and in the glands produces pictures of epithelial proliferation often closely resembling beginning carcinoma. At

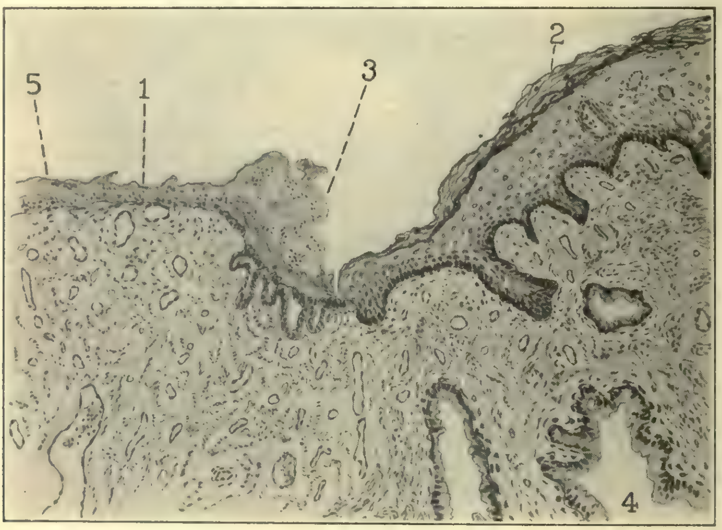

FIG. 147.—EDGE OF HEALING ULCER OF CERVIX. (H.P.) On the right the cornified surface epithelium joins in the center with the denuded ulcerating area. The denuded area is covered with exudate (fibrin, leucocytes), below this is granulation tissue (many thin-walled blood vessels). Below the exudate in the center is an area of ciliated columnar epithelium. This epithelium may be the precursor of normal squamous epithelium which marks the final stage of healing as in cervical erosion. 1. Exudate. 2. Squamous epithelium. 3. Columnar ciliated epithelium below exudate toward which broken line points. 4. Normal cervical gland. 5. Granulation tissue below entire area embraced between 5 and 3.

times the diagnosis is so doubtful that pathologists of experience and reputation will differ in their interpretation (see carcinoma of cervix, p. 271).

Ectropion is eversion of the cervical mucous membrane and its exposure in the vagina. Laceration of the cervix due to childbirth, gradual traction

from progressive prolapse which may open up the cervical canal as far as the os internum, or outward expansion as the result of swelling and edema in gonorrhea or other infections, produce the condition. Exposure to the acid vaginal secretion and various insults may cause chronic inflammation, ulceration or epidermoidalization.

12. **Tuberculosis of the Uterus.**—Tuberculosis of the uterus is but rarely primary. Kaufmann (123), Doederlein (124) and a few others believe that such cases have been authenticated. A most minutely executed autopsy in which no other tubercular foci are found, is necessary before such a claim can be considered. Ascending infections, if they occur, are also most infrequent and clinically negligible.

Secondary tuberculosis of the uterus is the rule. Most frequently direct infection from the tube takes place. Next in frequency hematogenous, or lymphatic infection from pulmonary, bronchial lymph-glandular, intestinal or peritoneal foci develops. In general miliary tuberculosis the uterus may be one of the organs involved.

According to White (125) the uterus is affected in 53 per cent of cases of genital tuberculosis and thus is exceeded alone by the fallopian tubes, 85 per cent. He also states that the uterine body is involved in 85 per cent, the cervix in 2 per cent and both in 13 per cent. This may be regarded as additional though indirect evidence in favor of the descending route of infection. The age affected is most frequently between 20 and 30 years, but reports of infants of 7 and 9 months (Schlimpert, Brüning, 126), and a woman of 79 years (Kaufmann, l. c. 123) show the two extremes. Of various predisposing agents gonorrhea, hypoplasia (Hegar, 127), and malformations (Merletti, 128), pregnancy and puerperium (Rosthorn, 129) are said to play some rôle. Of these the two last are alone of importance in the uterus, gonorrhea playing a decisive rôle in the tubes by creating a locus minoris resistentiae.

Uterine body.—In the early stages no macroscopic evidence of endometrial infection may appear. Usually, however, minute yellowish or whitish nodules can be seen in the mucosa. As the process advances confluence of the affected areas with caseation and ulceration develops. The uterine cavity is eroded by irregular ulcers with ragged, nodular masses, in between which are areas of reddish or yellowish to clayey-white tinge. If the cervical canal becomes impervious, as is common in the senile, accumulation of débris and pus may end in the development of a pyometra. The uterus may be thin-walled, and as the musculature is eventually invaded, in exceptional instances, perforation may result. A chronic fibrous type of endometrial tuberculosis is described by Williams (130).

The *histological* picture is in exact conformity with the gross appearance. In the early stage miliary tubercles are found lying in the stroma between the intact glands and beneath intact surface epithelium (Fig. 148). The tubercles are composed of epitheliod cells (large, poorly staining oval cells, with light oval nucleus) of connective tissue origin, amid which lie

giant cells. These giant cells may attain large size, their cell body takes the acid stains diffusely. The nuclei are numerous, oval, peripheral. Progression is marked by confluence of tubercles, by round-celled invasion and gradual loss of cellular definition (Fig. 149). The caseation shows itself by diffusely staining detritus, with some round cells and fibrin threads. The glands disappear and the surface epithelium is lost. The myometrium may also be invaded. As in other tubercular foci, lime deposits are not uncommon. Schroeder (130a) has studied 44 cases and believes that during menstruation infection of the deeper layers occurs.

Martin (131) demands the finding of tubercle bacilli to make a diagnosis. This appears an unnecessary, rigorous demand as no other uterine condition (except the almost unheard of one of gummatous endometritis)

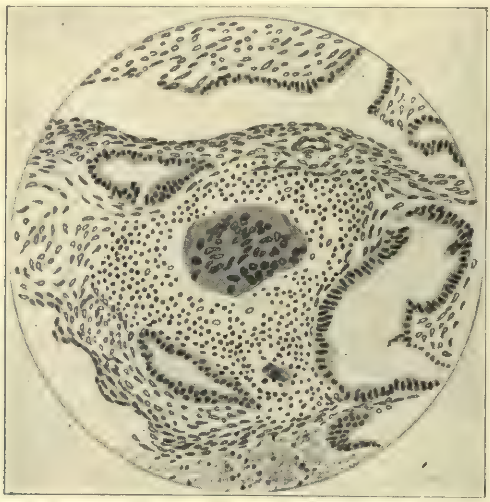

FIG. 148.—CURETTING FROM EARLY TUBERCULOSIS OF ENDOMETRIUM. (M.P.) Shows large giant cell surrounded by small round cells and normal uterine glands. This is the early stage in the miliary type.

resembles tuberculosis closely. In the diffuse, cheesy, advanced cases bacilli may not be demonstrable.

Metaplasia of the surface epithelium, stratification of the gland epithelia, are described by v. Franqué (132), Orthmann (133), as a response to the inflammation. Schottländer (134) inclines to the view that antecedent gonorrhea or pregnancy favors these changes which may even resemble the pearl formation seen in squamous carcinoma (Alterthum, 135).

Myometrial involvement is uncommon except as a final stage of the endometrial process. Kaufmann (l. c. 123, p. 1009) describes a case developing post partum, in which tubercles were found in close proximity to the blood vessels of the uterine wall, from which general miliary tuberculosis presumably developed. Mercadé (136) found five cases of myometrial

abscess. More rarely peritoneal tuberculosis succeeds in penetrating to some depth into the uterine wall.

Cervical tuberculosis forms about 8 per cent of all genital tuberculosis. In only 2 per cent is the uterine body not also involved. The portio is more often affected than the cervical canal (3 to 1) (Beyea, 137), but both together are often finally involved.

The process here also begins submucously in a miliary form (Cullen, 138). It may progress subepithelially for a long time, producing the rarely seen interstitial type (Fig. 150) in which the cervix enlarges diffusely, but the epithelium remains intact (Petit Dutaillis, 139). More frequently ulceration develops early. The undermined, dirty ulcers with grayish-yellow

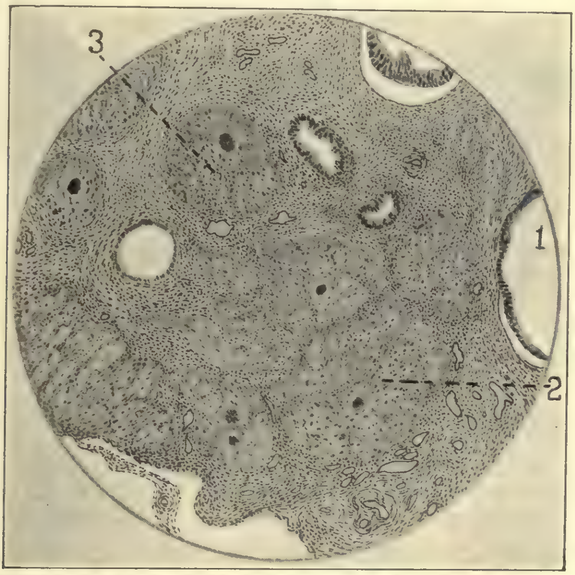

Fig. 149.—Curetting from advanced tuberculosis of the endometrium. (M.P.) Confluent and discrete tubercles composed mainly of epitheloid cells with a few gland cells are seen surrounded by the fibrous stroma of the endometrium. Remains of stroma can be noted within the tubercle. Glands stain poorly. There is no caseation. 1. Cystic uterine gland. 2. Confluent group of tubercles. 3. Discrete tubercle.

base, commonly situated about the external os, show tubercles at their base and edges (Vineberg, Moore, 140). They may cause extensive destruction resembling that of cancer and extend into the canal of the cervix and into the uterus. A papillary type in which the friable pink fungating masses may assume cauliflower, nodular or polypoid form also occurs (Chaton, 141). This may give rise to confusion with carcinoma or sarcoma (Emanuel, 142). The feel is soft and velvety and induration is lacking. The frequency of the various types as appearing in 77 cases was, predominantly ulcerating, 48; proliferative, 22; miliary, 7 (Châton, 141).

Perimetric tuberculosis is merely a manifestation of tubercular peritonitis. Diffuse crops of peritoneal tubercles or dense adhesions composed

of tubercular granulation tissue are found. Rarely the process may penetrate into the myometrium.

The writer (143) reported a case of intraperitoneal hemorrhage of unknown origin in which the possible source of hemorrhage seemed most likely to have been from tubercular adhesions on a large fibroid uterus.

Tuberculosis of the Gravid Uterus.—Tuberculosis of the placenta has been found in both general miliary and other forms of tuberculosis, or where no manifest signs were found in either mother or child (Weller, 143a). The tubercular foci most often occur in the intervillous space, next in frequency in the decidua basalis and least often on the fetal surface (Sitzenfrey, 144). Tubercle bacilli are most easily found by aid of the

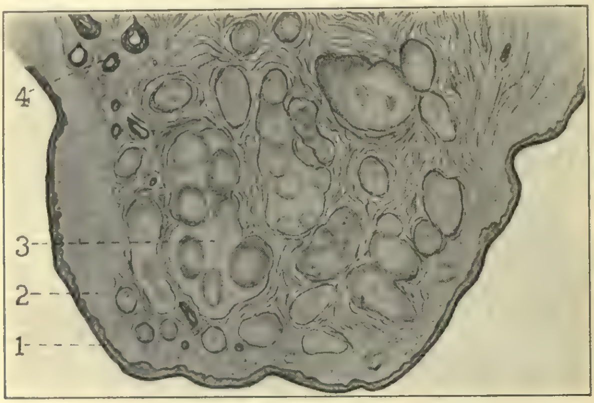

Fig. 150.—Tuberculosis of cervix. (Very low power.) Rare nonulcerating type. The cervix is riddled with tubercles. The surface epithelium is still intact. 1. Surface epithelium. 2. Diffuse tubercular tissue (epitheloid). 3. Caseating focus. 4. Normal cervical blood vessels.

antiformin method (Novak and Ranzel, 39 cases from the literature, 145). Bacilli have been found in the fetus (Schmorl, 146).

On the other hand, during pregnancy and especially in the puerperium, this includes the puerperium following induced abortion after the first few months—marked exacerbation of a tubercular process may occur. General miliary tuberculosis has been mistaken for puerperal sepsis. The spread may come from the uterus where penetration of enlarged vessels has taken place (Kaufmann, l. c. 123, p. 1009, Weil, 147).

The spread and exacerbation noted post abortum or in the puerperium according to v. Bardeleben (146a) is due to mobilization of the bacilli, when the placenta is expelled or removed. He therefore ablated the uterus with the pregnancy undisturbed, and later simplified the method by excising the placental site, thus reducing the mortality to zero (?).

Decidual tuberculosis is more frequent than placental. It is acquired during pregnancy. Diffuse caseation and nodular infiltration have been

described. It has been found as early as the fourth month (Runge, 148), and immediately postpartum (Schmorl and Kockel, 149), the woman having died of general miliary involvement. A diffuse tubercular endophlebitis of the uterine wall was described by Westenhöfer (150).

Kaufmann (l .c. 123, p. 1009) describes a case of chronic tuberculosis of the cervical canal which both he and Amann (151) consider the only case of primary uterine tuberculosis on record.

Tuberculosis in Tumors.—Carcinoma and tuberculosis have repeatedly been found together in the uterus (Fig. 226). See the literature in Schütze (152).

Adenomyomata have become tuberculous in some instances (Grünbaum, 153). Fibroids may be complicated by tuberculosis (Kelly, Cullen, 154), likewise uterine polyps (Zahn, 155). Vassmer (156) describes a case of uterine tuberculosis apparently cured by curettage, as the second curettage proved normal. The third shattered these hopes, material obtained again showing tuberculosis. This is not surprising when the fact that the uterus is rarely the only genital organ affected (11 out of 73 times) (Schlimpert, 126) is taken into consideration.

The writer believes he was more fortunate in the case of a young woman whom he first curetted and upon whom he then at once performed a double salpingo-oöphorectomy. The pyosalpinges were tubercular and endometrial tuberculosis was also found. A second curettage nine months later showed normal atrophic endometrium, but here the older tubal focus had been removed.

Except in pregnancy and in the puerperium extension of uterine tuberculosis (in fact, genital tuberculosis as a whole) to other systems practically never takes place (Kermauner, 157). Hence as the radical operations have a mortality of 10 per cent, Krönig (158) feels justified in advising medical observation or conservative operations.

Diagnosis will apply mainly to cervical types which are accessible to vision. In the earliest stages simple erosion may be simulated (Frankl portrays tuberculosis developing in an erosion, l. c. 45, opposite p. 104). Primary syphilitic lesions and ulcus molle, which may resemble early tubercular ulcers, should be readily recognized by aid of bacteriology. When the vegetative or destructively ulcerating forms resemble carcinoma, histological examination should prove conclusive. Enlarged tubes favor the diagnosis of tuberculosis. Corporeal tuberculosis, if the only lesion, will be recognized by means of the curettings.

13. **Syphilis of the Uterus.**—The popularization of the Wassermann reaction and improvements in the identification and growth of the spirochete (trepanomum) pallida in vitro will without doubt cast new light on syphilitic diseases of the uterus. Much of the older casuistic material must be discarded in view of our present knowledge.

Uterine body.—Hoffmann's (159) case alone seems fairly well authenticated. In a woman dying three months postpartum (from sepsis) the

entire endometrium was changed into a gummatous layer several centimeters in thickness, the process in spots extending into the myometrium. Similar gummata were found in liver and lung. Her twins showed no signs of syphilis, though the mother's Wassermann reaction was strongly positive.

The reports of Muratow, v. Jaworski, Whitehouse, Norris (160), and others in the main refer to syphilitic patients suffering from menorrhagia (often "fibrosis uteri"). Relief of symptoms from anti-syphilitic treatment does not signify uterine syphilis, nor do the scant histological reports substantiate the diagnosis.

Cervix.—The cervix is the site of syphilitic lesions in all three stages of the disease.

Chancre, the primary syphilitic lesion, is found according to Gellhorn and Ehrenfest (161) in 1.5 per cent, according to Oppenheim (162) in 8 per cent of all genital initial lesions. The types met with are, as elsewhere, simple, eroded, ulcerated or gangrenous. Induration of the base of the ulcer, and indurative edema of the cervix are constant. If the os is patulous the process may extend into the cervical canal. Favored by its protected situation, the chancre often heals rapidly, leaving no scar or trace (Gaucher, 163). Inguinal glandular enlargement is infrequent, as the cervical lymphatics drain into the pelvis. It is of extreme importance to obtain spirochetes from the lesions before secondary symptoms develop in order to abate the disease in the earliest stage (Fuchs, 163a). For histological details of the initial lesion see Vulva (p. 107).

In the *second stage* macules, papules and ulcers occur. These represent successive stages of development of the same lesion (Gellhorn and Ehrenfest, 161). According to Askanazy (164) a lymphocytic and plasma cell infiltration occurs around the dilated lymph and blood vessels. The epithelium is thickened, succulent and infiltrated with lymphocytes. Breaking down of the infiltrate produces ulceration, often with pyogenic infection superadded. Lesions occur within the cervical canal (Gellhorn, 165) and thus account for the spirochetes discovered in apparently normal cervical secretion (Gellhorn, l. c. Gräfenberg, 166).

In the *tertiary stage,* gummata may appear. They are not frequent. When present they rapidly break down (Neumann, 167), forming sharply defined, punched-out, dirty ulcers on the anterior or posterior lip. The ulcers may show a serpiginous advancement. In a recent case of Gellhorn's (168) invasion of the cellular tissues, erosion of the bone and a terminal peritonitis, due to retroperitoneal abscess, followed in quick succession from a large cauliflower tumor which had developed from a secondary cervical ulcer in spite of intensive treatment.

A recent monograph by Ozenne (168a) gives the full literature of uterine syphilis.

Gummata are not always histologically characteristic. Again quoting from Askanazy (164) (p. 188) gummata contain many lymphocytes, fibroblasts and a fibrous ground work. In spite of necrosis some trace of

the preëxisting structures can be recognized such as connective tissue strands, vessels and cell groups in which the nuclei do not take the stain. Epitheloid and giant cells are inconstant.

Syphilis of the Gravid Uterus.—No lesions characteristic of syphilis of the maternal tissues, the decidua basalis and capsularis, have stood the test of modern critique. *Endometritis deciduae polyposa et tuberculosa,* "gumma" of the decidua, leucocytic infiltrations have been shown not to be specific. For literature see L. Seitz (169).

Chancre of the cervix during pregnancy may show undue persistence (up to five months) and can, by producing boardy induration, prove an absolute bar to spontaneous delivery (Lantuéjoul collected seven cases, 169a).

On the other hand, by means of the Wassermann test and the finding of spirochetes, syphilitic lesions of the placenta have been put on a firmer basis. The gross signs are not constant. This was shown by Mracek (170) who, in 160 placentae of surely syphilitic mothers, found no macroscopic signs in 82. Disproportionally high weight of the placenta (1 to 5, even 1 to 3) is also not limited to syphilis (Labourdette, 171). Therefore neither excessive weight, pale appearance or greasy maternal surface are pathognomonic. The last two are present whenever fetal death occurs a few days before birth, and are due to cessation of circulation (Frank, Merttens, 172). The omphalitis described is also not characteristic. Slemons (173), who has done much to clarify the entire subject, says that syphilitic infiltration appears at the fetal end, placental bacteremia producing lesions at the maternal end. His histological examinations of the placenta in 99 per cent were concordant with the Wassermann tests (360 cases examined, positive test in 10).

According to Slemons the test described by Frankel (174) in 1873, is still the best. Fresh placenta is teased in dilute hydrochloric acid or in water. Under the microscope the syphilitic villi appear abnormally large, opaque and irregular in shape, with swollen ends. Characteristically, the branching is limited and the blood vessels are indistinct.

In cut and stained sections the almost complete obliteration of the intervillous space due to the increase in size of the villi, the inflammatory reaction in the intima and media of the vessels of the villi, the cellularity of the stroma and the apparent invasion of the stroma by the syncytial layer bespeak syphilis. v. Franqué (175) and also Hitschmann and Volk (176) do not agree to the specificity of these findings.

Spirochetes have been found in the placenta even after intensive search, in only about every third case of syphilis (Bab, 177; Gräfenberg, 166). Emmons (178) has found it difficult to demonstrate the spirochetes in the cord. Therefore, as heretofore, reliance will have to be placed in the majority of cases upon the histological changes.

Diagnosis.—Primary and secondary lesions on the cervix should be at once confirmed as syphilitic by means of demonstration of the pale spiro-

chetes by the dark field or India ink method. Ulcus molle or pyogenic infection added to the chancre may becloud the gross appearance, but do not affect the recognition of the spirochetes. In tertiary lesions tuberculosis and cancer will require differentiation; usually the histology is at once decisive in both. If doubt as to possible tuberculosis exists, staining for tubercle bacilli, if positive, is conclusive. If negative, a positive Wassermann reaction, gummata elsewhere, locally absence of numerous giant and epitheloid cells, and sharply demarcated caseation speak for syphilis.

The characteristics of placental syphilis have been sufficiently emphasized.

III. ADENOMYOMA OF THE UTERUS AND RECTOVAGINAL SEPTUM AND OF OTHER REGIONS

Adenomyoma is a diffuse growth containing glands lying either in a fibrous or cytogenic stroma, surrounded by unstriped muscle. It resembles a diffuse myoma with islands of uterine mucosa scattered throughout it (Cullen, 179). The gland structures, moreover, whether the location is uterine, rectovaginal (Curtis, 180), ovarian, round ligament (Casler, 181) or umbilical (Cullen, 182) show evidence of menstrual bleeding. The sites in which these growths have been found is shown in Fig. 151, taken from Cullen.

Adenomyoma of the Corpus Uteri.—Cullen (183) in 1283 cases of myoma found adenomyoma in 73, about 5.7 per cent. At the Mayo clinic (MacCarthy and Blackman, 184) in 3398 fibromyomata, 211 were adenomyoma, about 6.4 per cent. The disease is most prevalent between the ages of 30 and 60 years, and of the Mayo patients 65 per cent of the married had borne children. The disease may manifest itself in the form of discrete rounded myomata, or as a diffuse, even enlargement of the uterus with or without submucous polypi or subserous growths. In either case no capsule formation takes place and the affected areas cannot be shelled out of their bed as ordinary fibromyomata are removable. Adhesions to the uterus are often present.

On opening the uterus the adenomyomatous areas show as coarse striations enclosing gray-blue, slightly sunken, more translucent areas. Often small cysts with chocolate-colored contents are scattered throughout. The diffuse variety may completely surround the endometrial cavity like a second mantle of endometrium; it may communicate in numerous spots with the endometrium and may extend outward to the serosa. The demarcation line between diseased and normal musculature is sharply defined.

The *histological picture* in a typical case is very characteristic. The uterine mucosa remains normal, but the mucosa is seen to penetrate in all directions toward the underlying diffuse myomatous tissue. If the interstices are narrow, only individual glands, if wide, large areas of mucosa penetrate

into the depth. Occasionally it is possible to follow such prolongation of the mucosa half way through the uterus. Where the diffuse myomatous growths end, the outward extension of the glands end likewise (Cullen, 179). In less typical cases a few scattered glands may be found throughout a fibromyoma but the absence of capsule and difficulty in shelling out such a growth is present.

FIG. 151.—THE ABNORMAL DISTRIBUTION OF UTERINE MUCOSA. 1. In the wall of the uterus and at the uterine horn. 2. In the rectovaginal septum. 3. In the round ligament. 4. In the ovary. 5. In the utero-ovarian ligament. 6. In the uterosacral ligament. 7. At the umbilicus. The uterine glands with their stroma are usually embedded in nonstriped muscle and fibrous tissue. (From Cullen, *New York State Jour. of Med.* Aug. 1919.)

The gland epithelium is low cuboidal to cylindrical with an oval deeply staining basal nucleus. Cilia may be found. The stroma is either purely fibrous and may be scant so that the glands are in immediate apposition with muscle (Fig. 152B), or may be cytogenic (Fig. 152A). The cyst content contains mainly disintegrated old menstrual blood, which is retained in these cavities.

Blair Bell (185) operated upon such a growth during the second day of the menses and describes the menstrual picture in its glands. Amos (186)

reported an adenomyoma with decidual changes in it. T. O. Döderlein (187) and Herzog (187) found nidation in an adenomyoma, the placenta lying in a secondary cavity communicating with the uterine cavity by a narrow canal. Kelly and Cullen (187a) describe tuberculosis in an adenomyoma, as does Lindquist (187b).

Adenomyoma of the Rectovaginal Septum.—The disease begins as a small nodule on the posterior surface of the cervix in the subperitoneal tissue of the cul-de-sac. At first the rectal mucosa is movable over the mass. With continued growth extension laterally into the broad ligaments, downward into the rectovaginal septum, intimate adherence with the rectal wall develop. Vaginal polypi appear and the vaginal wall may be penetrated (Cullen, 188; Curtis, 180). Such penetration is marked by normal-

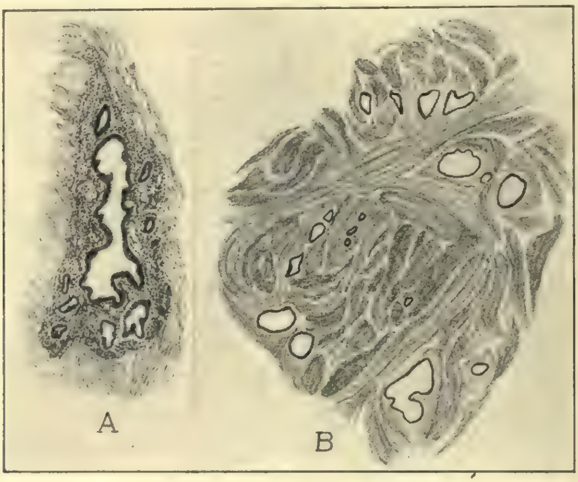

FIG. 152.—(A) ADENOMYOMATA WITH UTERINE GLANDS SURROUNDED BY TYPICAL CYTOGENIC STROMA. (M.P.) (B) Slightly lower power, shows second type of adenomyoma. In which the glands abut directly against the uterine musculature without interposition of cytogenic stroma.

looking uterine mucosa lining portions of the vaginal vault and a menstrual flow continues even after the uterine body has been removed by hysterectomy (Cullen, 188; Curtis, 180). The tumor enlarges during the menstrual period and causes increased compression symptoms at that time. Eventually the pelvis may be blocked by the growth, death resulting from the increased hemorrhages and partial intestinal obstruction.

Histologically these growths likewise correspond to uterine glands with stroma and unstriped muscle tissue, with a tendency to cyst formation and hemorrhages. Due to their exposure to infection and trauma they may contain more evidence of inflammation, i.e., round and plasma cells, than the other types show. Decidua formation was found by Griffith in a case of a woman near term.

Adenomyoma of the Tubal Angle.—Small discrete enlargements from pea to cherry size are found at the beginning of the fallopian tube. The nodules are made up of glandlike structures with fibrous stroma and some unstriped muscle fibers. They are usually noted in connection with inflammation of the tube (v. Franqué, 189), not infrequently of tubercular origin (Rabinowitz-Robinson, 25 per cent, 190. See Fig. 251, p. 345. They may regress as the inflammation subsides. v. Recklinghausen (191a) regarded them as due to wolffian rests.

Adenomyoma of the Round Ligament.—Nodules have been found along the course of the round ligament, most often near the external ring. These small masses may enlarge during menstruation. They form dense adhesion to the fascia. Their histology is similar to that of other adenomyomata (Cullen, 191; Sitzenfrey, 192). Martin (see Chapter XII) removed a pedunculated mass containing 12 liters of chocolate-colored fluid. The pedicle arose from the left round ligament. Mahle and MacCarthy (192a) report two cases in the groin unconnected with the round ligament.

Adenomyoma of the Utero-ovarian Ligament.—Adenomyoma of the utero-ovarian (Cullen, 183, p. 40; Frankl, 193) and of the utero-sacral ligaments are infrequent, unimportant, accidental findings.

Adenomyoma of the Umbilicus.—Small tumors of the umbilicus are found, covered with normal skin, in some instances enlarging during menstruation (see Cullen, 182). The histology is identical with that of other adenomyomata. Mahle and MacCarthy report one case (192a).

Adenomyoma of the Ovary.—Under the caption of "uterine mucosa in the ovary," Cullen describes the findings in four cases. In two of them, islets of normal uterine mucosa were scattered throughout the ovary; in the third a small cyst was lined with it.

The fourth case reported by Casler (181) is one in which a uterus was completely removed. The tumor was formed by a "diffuse myomatous thickening and scattered throughout this diffuse growth were quantities of stroma identical (?) with that of the uterine mucosa. This stroma, however, contained no glands." The patient continued to menstruate regularly through the vaginal vault. After 3½ years, one ovary which had been left behind began to enlarge. When removed 4 years after the first operation, it was as large as a grape fruit. "Great quantities of typical uterine mucosa were found scattered throughout the ovarian tumor, thus clearly explaining why the patient had continued to menstruate without any uterus."

The earliest report is that of Russell (181a). In addition to these, Cullen reports C. C. Norris' case (Proc. Path. Soc. Philadelphia, N. S. XII, Old S. XV, Jan. 1919–20) and a case of O. Schwartz (181b).

Pick (181c) described four cases, in one of which the ovaries were normal in size, in the three others bilateral growth of "goose-egg to apple size" existed. He called the condition "Adenoma endometroides ovarii" and suggests its possible identity with Rokitansky's "cystosarcoma

adenoides ovarii uterinum" (Lehrb. d. path. Anat. 1861. Vienna, 3d Ed. III, 423, 431).

Pfannenstiel (Veit's Handbuch IV, i, page 174) records a case, Rabinowitz-Robinson (181d) another.

Thus, largely through the efforts of Cullen, adenomyoma of the genital tract has been welded into a clinical and pathological entity characterized by the presence of tissue identical in histology with that of the uterine mucosa, partaking of its physiological function in regard to menstruation, and possibly accounting for the ability of the ovum to nidate ectopically (?). Are such adenomyomata of uniform origin? v. Recklinghausen (191a) derived especially the adenomyomata of the tubal angle from mesonephric rests. This origin was championed by Pick (194). The resemblance of some glands to glomeruli of the mesonephron (pseudoglomeruli) the arrangement in comb-like distribution of ductlike glands, the muscle mantle around the glands, were all cited in substantiation (see Lit. Ernst, 195). R. Meyer (196) is willing to concede such origin in only one case in which the structures resemble the adult epoöphoron (see Fig. 58, p. 67).

Both mesonephric and wolffian derivation have been claimed for the tumors of the round ligament, utero-ovarian ligament (Emanuel, 197; Chevassu, 198), and of the rectovaginal septum (Pfannenstiel, 199; Pick, 194). v. Babo (200) ascribes adenomyoma of the ovary to mesonephric rests.

A müllerian derivation from embryonal rests or postembryonal sprouts of the gland epithelium (Babes, 201; C. Ruge, 202) has gained more credence. Robert Meyer (196, page 472) presupposes miliary abscess formation in the muscular wall, with subsequent ingrowth of mucosal glands into the granulation tissue between the muscle bundles. Such origin may apply to a small fraction of cases, but in the majority the cause is unknown. In certain locations, as in the tubal angles, where preceding inflammation is common, in the diffuse growths encircling the endometrium (adenomyositis) in which the uterus is often densely adherent to adjacent organs, an inflammatory origin is plausible (v. Franqué, 189). In discrete tumors the same cause that produces the myoma part of the growth (ovarian?) may be causative. Glandlike downgrowth of the peritoneal epithelium has been noted in many instances as result of inflammation (Iwanoff, 202a)—uterine serosa, ovary, peritoneal adhesions anywhere, or transplanted into the scar of a laparotomy wound (Klages, 202b) (see Fig. 153). R. Meyer (196, p. 472) derives the adenomyomata of the rectovaginal septum from such downgrowths into granulation tissue of Douglas's cul-de-sac, in which large numbers of round cells and plasma cells occur. Any explanation will fail to be convincing unless it accounts for the widespread occurrence of gland structures functionally equivalent to those of the uterine mucous membrane.

Adenomyomatous growths of the cervix may be derived from Gärtner's duct (Thumin, 203). Cyst formations from this source are, however,

more usual. Implication of the cervix as well as the rectovaginal septum by adenomatous growths were noted by Kleinhans (204) and Sitzenfrey (205).

Rarely carcinoma arises from adenomyomata (Meyer, 196, p. 483; Polano, 206; Sitzenfrey, 205; Dillmann, 207). A sarcomatous adenomyoma was reported by Bauereisen (208). Pick (209) and Wiener (210) described adenomyoma psammopapillare.

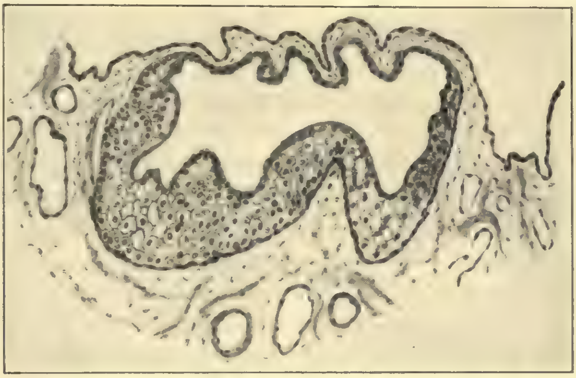

FIG. 153.—"PERITONEAL GLAND" SHOWING POWER OF PERITONEAL ENDOTHELIUM TO PROLIFERATE. (H.P.) Above is a thin layer toward the free peritoneal cavity. Lower part of the gland is lined by multilayered cells. Below is vascular subperitoneal stroma.

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CHAPTER VIII

TUMORS OF THE UTERUS EXCLUSIVE OF ADENOMYOMA

I. MYOMA OF UTERUS

(Fibromyoma, Fibroid, Leiomyoma)

Mallory (1) justly declares that the term "fibromyoma" would be applicable to a mixed tumor, but is incorrect when used to designate simple tumors, such as myoma of the uterus, in which the connective tissue acts merely as a supporting substance. However, the term "fibromyoma" and "fibroid" are so generally accepted and employed, that the writer will not essay the thankless task of reforming the nomenclature and will use these terms interchangeably with myoma to designate the tumors composed of unstriped muscle fibers occurring in the uterus and other portions of the female genital tract (vagina, tube, ovary, round ligament).

Etiology.—Age.—Fibromyomata are rarely seen before puberty. They appear with increasing frequency during the more advanced decades of sexual activity—20 per cent after the 35th year according to Bayle (2) and 40 per cent after the 50th year according to Klob (3).

Those of Senator and Kaminer (4) of 11 per cent agree closely with autopsy statistics of Welch (vide infra). Among gynecological cases according to Hofmeier (5) and Essen Möller (6), calculated from respectively 11,073 and 11,203 patients, fibroids formed 4.3 to 4.7 per cent. Welch's autopsy records as quoted by Kelly and Cullen (7) among 742 females showed 148 myomata, or 20 per cent. Of these, white women formed 10 per cent and negresses 33.7 per cent, emphasizing the proneness of the colored race to fibroids of the uterus.

The *frequency of occurrence* at various ages is well illustrated by statistics gathered by the writer in 406 consecutive cases of fibroids (Frank, 8), those of McDonald (9) covering 700 cases, and of Kelly and Cullen (7) including 1285 cases.

Ages	*Frank*	*Kelly and Cullen*	*McDonald*
20–30 years	64–15.5%	153	19– 2.7%
31–35 "	65–15.5%	225	
36–40 "	100–23.0%	324	233– 33%
41–45 "	84–20.0%	274	
46–50 "	62–15.0%	196	332–47.6%
51–60 "	21– 7.5%	101	95– 13%
60–70 "	10– 3.5%	12	21– 3%
	406	1285	700

The high age incidence between 20 and 30 years in the writer's series is borne out by a large policlinical material (in which few colored women figured), the exact figures not being available at this time. It contrasts with that of most observers, Giles (10) 8.7 per cent, Essen-Möller (6) approximately 7 per cent, Gusserow (12) 17 per cent. In all the statistics the fastigium is reached between 30 and 50. Thereafter a sharp drop occurs.

Fertility.—It would also appear that fibromyomata occur more frequently in the nulliparous than in the parous woman. Essen-Möller (6) in 11,000 patients found one virginal to four non-virginal in his gynecological patients; in 530 fibroid bearers, 1 virginal to two non-virginal. Giles (10) finds similar conditions up to the age of 40 years; thereafter the reverse order obtains.

The absence of *pregnancy* may be said to predispose to fibroid formation, the myomata appearing after 10 to 20 years of sterile married life (Hofmeier, 5). When present, however, a distinct reduction in fertility was noted (22 per cent), Blumreich (4) p. 720, 29 per cent, Giles (10) page 124. The effects of pregnancy on fibroids will be discussed in succeeding paragraphs, while the effects of fibroids on pregnancy and labor will more properly fall to books dealing with obstetrics.

Causation is as unknown as that of other tumors. Heredity, if at all, plays a very minor rôle (Kelly and Cullen, 7, page 430), although fibroids may appear in many members of the same family.

Veit (13) ascribed some importance to sexual irritation (masturbation, coitus interruptus) by which congestion is kept up. The monthly growth impulse, undergone by the uterus in response to ovarian stimulation, more probably accounts for the occurrence of myomata during the period of sexual activity. An altered hormone secretion such as Seitz (14) presupposes is not necessary in this conception.

Histogenesis.—Although many theories exist, nothing definite is known. Virchow (15) believed that any muscle fiber of the uterus, Ribbert (16) that certain fibers which have never been in complete connection with the normal complex, Cohnheim (17) that unused embryonal rests form the basis of fibroid tumors. Roesger (18) derives myomata from the small blood vessels of the uterus. Gottschalk (19) finds the beginning of the tumor in the tortuosities of the central arteries of the minute myoma. R. Meyer (20) more recently inclines toward a combination of Cohnheim's and Virchow's views, showing specimens with uninterrupted transitions from normal to myomatous muscle fibers. None of the hypotheses have any real anatomical basis.

Site.—Myomata may occur in any portion of the uterus. They may be "seedlings" of microscopic size, or gigantic masses like the fibroid weighing 140 pounds described by Hunter (21). A solitary fibroid is not uncommon; on the other hand uteri whose walls are completely riddled with myomata, whose surface is studded with innumerable growths are frequent.

Consequently the variations in size, shape, disturbances produced and outcome are protean.

The vast majority of myomata begin intramurally. They may remain in this location (interstitial) or extend outward toward the peritoneal surface, becoming subserous, or inward toward the uterine cavity, becoming submucous. Subserous and submucous growths evince a tendency to pedunculation. Usually the intramural origin of a tumor shows itself by at least a thin shell or cap of musculature which remains even after the growth has become submucous or subserous. At times the shell may atrophy completely, thus affording no guide as to the site of origin. A small number of fibroids begin in the mucosa, a somewhat larger number originate immediately beneath the peritoneum Lockyer (21) appears to go too far in saying that in the uterus, "they are invariably intramural," while Frankl (22) attaches an unwarranted importance to the frequency of extramural origin. The relative frequency in situation, according to v. Winckel (23), of intramural, subserous and submucous growths is as 65: 24.3: 10.7.

Both clinically and anatomically great differences result from the exact location of the fibroid. *Corporeal* fibroids develop into the three varieties above mentioned, except when the growths are situated along the lateral uterine wall. They then separate the layers of the broad ligament and become intraligamentous. A fibroid may develop in such a fashion as to be intraligamentous and subserous at the same time, or partly intramural and submucous, etc.

Cervical fibroids except such which arise high upon the posterior surface of the cervix and grow upward into the cul-de-sac, in which case they may be subserous, are subperitoneal, or retro-peritoneal if centrifugal in development. They become submucous, when developing into the canal. More rarely fibroids develop from the infravaginal part, the portio, and grow into the vagina. Cervical myomata form only about 7 to 8 per cent of all fibroid tumors (Amann (25) 2 per cent, Balaban (26) 5 per cent, Frankl (24) 6.94 per cent).

Interstitial myomata remain within the uterine wall, which hypertrophies around the growth. In consequence, even if single, great distortion of the uterine cavity may result (elongation, increase in width). These tumors are usually spherical.

Subserous myomata originate as sessile growths. Many become pedunculated, in which case, even if of large size the size and shape of the uterus is little affected. They often are hard and fibrous. The pedicle may elongate so as to allow great freedom of excursion, torsion of the pedicle, with consequent strangulation, necrosis or calcification. Usually under these conditions adhesions secondarily develop affording nourishment. Such myomata are called parasitic. They may lose their original point of attachment completely and become wandering (Gouillond, 27).

Submucous myomata in most instances begin as intramural tumors. As they grow into the uterine cavity, contraction of the uterine muscle tends to

extrude them into the lumen. Hence pedunculation or polypoid form develops early. Small growths have thin pedicles, are usually forced through the cervix and borne into the vagina, or remain like a ball valve within the cervical canal (hour-glass shape), or appear intermittently at the external os. Large growths even if pear-shaped and partly pedunculated have a broad base.

So-called *"recurrent fibroids"* which appeared in the older literature were usually sarcomata. However, rapid growing simple submucous myomata may act similarly. Kelly and Cullen (7, p. 179) report a case in which at intervals of 3, 2, and 3 months sloughing pedunculated fibroids 9 and 10 cm. in diameter were found projecting into the vagina and removed. The patient has remained well.

The mucous membrane over the convexity of the growth, and on the opposing uterine wall, or where multiple submucous growths touch and face each other, is thin and atrophic. Quite rarely attachment of the surface to the opposite uterine wall, or even to the vagina has occurred. (Leyden, 28). In the interstices between tumors and wall hyperplasia of the mucosa is noted. Sometimes the apex of a polyp is denuded of mucous membrane (trauma if born in vagina, necrosis, etc.). Hence infection, sloughing and gangrene is a not uncommon sequel. On the other hand, an exposed polyp may show epidermoidalization where exposed to insult. Small cysts may appear on its surface. Rarely spontaneous expulsion of submucous fibroids occurs. They have been known to be born in front of an advancing fetal head. Inversion of the uterus may result from traction (see p. 176).

Subperitoneal (or retroperitoneal) myomata include the intraligamentary, and all cervical fibroids except those growing upward through the posterior cul-de-sac.

Intraligamentous tumors may spread apart the layers of the broad ligament, displacing the uterus toward the opposite side and upward. They may grow upward into the layers of the mesosigmoid, displace the cecum or grow downward, becoming indistinguishable from cervical myoma. Blocking of the pelvis, displacement of the uterus, bladder and rectum are frequent sequelae. The tumor may lose its attachment to the uterus and appear as a fibroid arising from the broad ligament.

Interstitial cervical myomata displace the uterus upward (Fig. 154) so that the corpus rides on top of the growth, the cervical canal elongates enormously and assumes the shape of a scabbard. Centrifugal growths develop subvesically, or become paravaginal or rectal. Centripetal development produces sub-mucous tumors, which, until the site of origin is located, are indistinguishable from uterine polypi. Large growths completely filling the vagina may develop from the anterior or posterior cervical lip (Kolb, 29). For literature of cervical fibroids see M. Rabinowitz-Robinson (30), Balaban (26).

Migratory Uterine Fibroids.—Occasionally a uterine fibroid through

mechanical causes (torsion, etc.) gradually loses its attachment to the uterus and derives its nutrition from other intra-abdominal organs. Peterson (30a) describes cases illustrating all stages of the process and records 20 cases from the literature.

1. **Gross Anatomy of Fibroids.**—The various shapes assumed by fibroid tumors have been sufficiently described in the preceding paragraphs. The consistency and color of the growths depend largely upon the relative amount of muscle and fibrous tissue. If muscle preponderates the tumors are soft, elastic and of pinkish tinge; if the fibrous tissue is in excess the

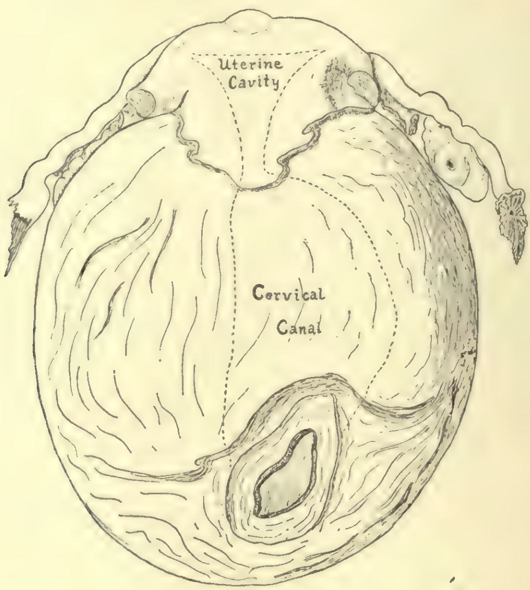

FIG. 154.—SUBPERITONEAL CERVICAL FIBROID. ($\times\frac{1}{3}$.) Showing fundus of uterus riding upon the tumor. The distorted flattened cervical canal has assumed scabbard shape. A recently ruptured corpus luteum is seen in the left ovary.

growths are hard and white in color. Other factors such as degeneration, torsion of the pedicle, or infection, may, however, alter these properties. The fibroids are (except when so-called carneous degeneration has taken place) always strongly contrasted against the normal uterine muscle, which is pink in comparison.

On section the surface has the appearance of watered silk and is seen to be composed of single or multiple nodules arranged without regularity. Discrete, intercommunicating or gyrate areas are found. As a rule the smaller the myoma the less the capsule formation is in evidence. Microscopic nodules have no capsule. Large growths, if growing mainly from the center, are lamellar at their margin and largely by pressure, partly by hypertrophy of the neighboring uterine muscle, form a concentric capsule (R. Meyer, 20) (Fig. 155). The parallel fibers and muscle bundles are united here and there by connecting bridges and upon maceration or dissection show the so-called muscle-

rhomboids (Gebhard, 31). Where the fibroid grows mainly from the periphery no distinct capsule may be formed.

Histology.—Myomata are very simple in structure, consisting of interlacing bundles of unstriped muscle supported by more or less fibrous connective tissue.

The smallest myomata, of microscopic size, consist of unstriped muscle differing from the normal uterine muscle only in deeper staining qualities, and often showing direct continuity with normal cells (R. Meyer, 32). Little, if any, connective tissue

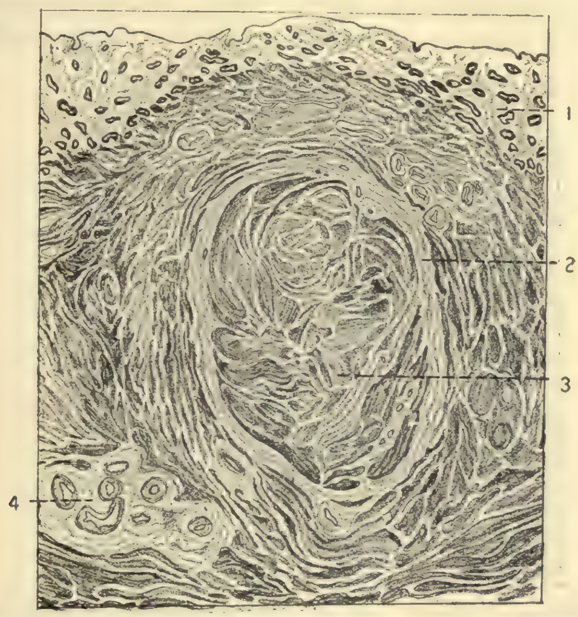

Fig. 155.—Small interstitial fibroid. (×6.) The fibroid is developing toward the uterine cavity, but is still separated from the mucosa by a thin layer of muscle. Size 1 × .7 cm. Capsule fully developed. 1. Mucous membrane of uterus, toward center slight thinning of mucosa due to compression. Note horizontal course of glands. 2. Connective tissue of capsule of fibroid. 3. Muscle bundles of fibroid cut across at various angles. 4. Large nutrient vessels of fibroid situated in the uterine musculature.

and an entire absence of capsule are noted at this stage. Slightly later, cleavage spaces, often lined with endothelium, can be seen at the edge and the "pedicle" or connection with the normal uterine muscle disappears.

With continued growth, especially if proceeding from the center, the outer layers of the myoma as well as the adjacent uterine musculature arrange themselves in concentric lamellae and thus form the capsule, which is composed of both tumor and uterine tissue. In the capsule will be found the nutrient vessels, which may run along the surface of the growth, divide and send branches into the depths of the tumor along the septa which increase continually in number as the tumor ages. Myomata are commonly

not well supplied with blood vessels. This accounts for the frequency of degenerative changes.

The smooth muscle cell of the myoma according to Hertz (33) ordinarily varies from 0.045 to 0.255 mm. in length but exceptionally attains 0.350 to 0.480 mm. . It is elongated, usually spindle-shaped, narrow, ending either in a point or bifurcation. The cells lie closely packed, side by side. They stain deeper than normal cells (both nucleus and protoplasm). Van Gieson's stain colors the muscle fibers yellow, the connective tissue red. Within the cell body fine longitudinal striations (Binnen fibrillen, Benda) and externally coarser *myoglia fibrilles,* which project beyond the cell and interlace with the fibrilles of neighboring cells can be demonstrated by

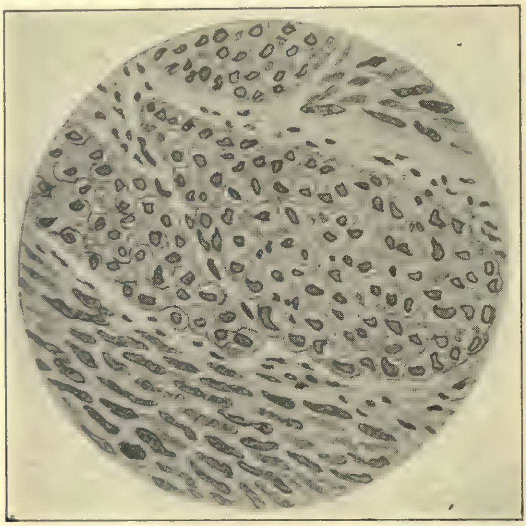

FIG. 156.—FIBROMYOMA. (Medium power.) Muscle bundles cut transversely, obliquely and longitudinally. When transversely cut the nuclei appear as dots and the cell body shows hexagonal outline. Longitudinally cut the nuclei appear elongated with transverse markings and the cell body shows a fibrillar wavy line. Between the muscle bundles is connective tissue.

special stains (Mallory's or Benda's), Heimann (34). Occasionally they become apparent with simple stains (see Fig. 156), especially in pregnancy.

The nucleus is longer than that of an ordinary muscle cell, has blunt ends and frequently is wavy or spiral. Therefore in oblique section it may appear as a long oval; in cross section it shows as a round, oval, or half-moon shaped body with sharply defined cell membrane. Often the cells appear empty, the section not passing through the nucleus (Fig. 156). The nucleus contains 2 or 3 nucleoli. Mitoses usually signify malignancy. Gottschalk describes direct cell division (19). This observation is unconfirmed.

The connective tissue cells send fibrilles between the muscle fibers, intrafasicularly, and separate the muscle bundles by forming septa (Figs. 155 and 156). In young growths the cells are numerous, spindle-shaped, with

oval nuclei. The older the connective tissue, the less cellular it becomes. Elastic fibers increase in the older tumors.

Although the smaller blood vessels show an absence of adventitia and their media abuts directly against the muscle cells of the myoma, as described by Roesger (18), no histogenetic importance can be ascribed to this lack (Fig. 157).

Mast cells are found in myomata, especially in the adventitia and about vessels but importance is no longer attached to their presence (Gebhard, 31, page 100). Nerve fibers are regarded as chance inclusions.

2. **Changes in Myomata.**—Changes, especially hyaline degeneration is frequent in myomata. Kelly and Cullen (7, page 83) found readily

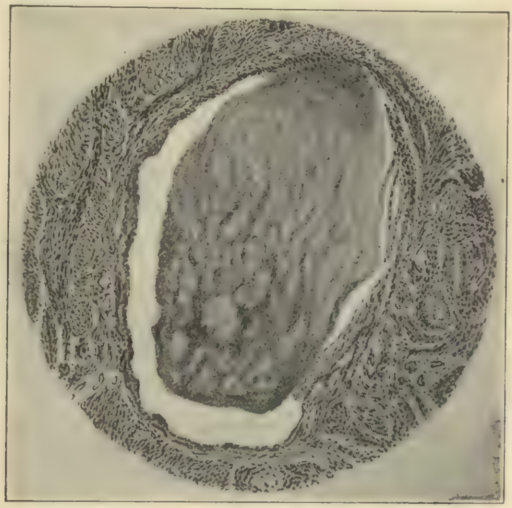

FIG. 157.—VEIN OF NECROTIC FIBROID. (Low power.) A large thin walled vessel is shown, its walls closely attached to the muscle tissues of the fibroid. Within the lumen is a large occluding thrombus, adherent to part of the vessel wall. The necrotic area begins immediately beyond the part shown in this illustration.

recognizable hyaline changes in 114 out of 1674 cases. Lockyer (21, page 192) claims that large myomata always show hyaline changes and small ones often do the same. Piquand (35) states that they occur in 30 per cent.

ATROPHY.—Atrophy is of rare occurrence and may be due to diminished circulation either occurring spontaneously, as the result of X-ray treatment (Meyer, 36), operative castration (Döderlein and Krönig, l. c. (37) p. 529, full lit.), or the menopause. The tumors shrink and become scarlike. The individual muscle cells show fatty degeneration, the connective tissue becoming preponderant (Gebhard, 31, page 109).

CIRCULATORY DISTURBANCES.—These may result from gross causes such as torsion of the pedicle in a subserous myoma, or constriction exerted by the cervix in a case of pedunculated submucous fibroid either partly or

completely borne into the vagina. More commonly the venous return is impeded where the veins, after coursing along the surface of the tumor, enter the capsule. Very slight gliding of the layers at this location will produce the kinking. Thrombosis of capsule veins, or veins within the tumor is frequent (Fig. 157).

As a result of these and other lesions congestion and stasis, edema, hemorrhages into the tissues of the tumor, and various degenerations result. Rarely massive intraperitoneal hemorrhage results from rupture of the thin-walled vein on the surface of a myoma (Stein, 38, Benzel, 39). Death from bleeding from a submucous polyp is also recorded (Jolly, 40).

FIG. 158.—FIBROID WITH HYALINE DEGENERATION (ANGIO FIBROMA). (Medium power.) The fibroid is extremely vascular. Around each vessel, formed by the media and adventitia, are hyaline areas in sharp contrast with the very cellular myomatous tissue lying between the vessels. These characteristics produce a superficial resemblance to an angio-sarcoma. The capsule on the right is normal.

Rarely thrombophlebitis occurs with fibromyomata (Sitzenfrey, 41). Post operative thrombosis and embolism is more frequent after hysterectomy for fibroids than after any other operation. The thrombosis, especially of the femoral veins, may develop in from one to three weeks after operation. Embolism may occur without noticeable symptoms of thrombosis. Baldy (42) recorded 366 cases of myoma with 13 sudden deaths, there being only three such deaths among 3047 other gynecological cases. Burkhard (43) in 236 operations for myoma records twelve thromboses with six ending in fatal embolism, Lindquist (44) in 186 hysterectomies sixteen thromboses and two fatal embolisms.

Edema must be differentiated from lymphangiectases (in the latter endothelial lined cavities), clear or straw-colored fluid exuding in both

instances upon laying open the growth. Rarely telangiectatic or cavernous myomata are encountered. A case of the latter with hyaline degeneration superadded is shown in Fig. 158. Kelly and Cullen (7) describe a fibroid with multiple angiomatous foci.

Hyaline Degeneration.—This degeneration is common. It appears either in widespread or discrete areas in most fibroids. The tumor may in consequence become harder or softer, cartilaginous or pulpy in consistence and may be succulent or cystic, depending upon the extent and stage of the change. The color is whitish yellow, or when blood tinged assumes darker shades. Macroscopically the area may resemble fat (Kelly and Cullen, 7).

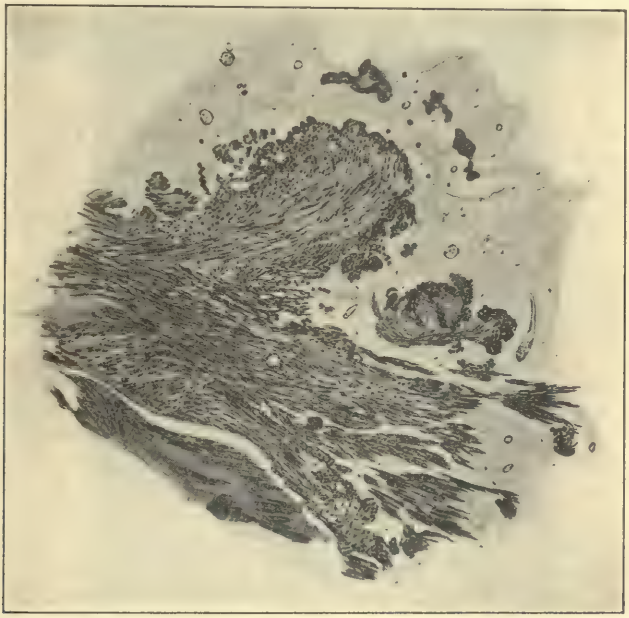

Fig. 159.—Fibroid with beginning hyaline degeneration. (Medium power.) Above, acellular area of degeneration containing here and there well preserved small blood vessels and bundles of swollen muscle. Below and to the left the musculature of the fibroid is normal, with increasing degeneration toward the right margin.

At first the connective tissue, later the musculature becomes homogenious and acellular (Fig. 159). The consistence is then hard. Individual muscle bundles or fibers may survive and the blood vessels resist the process longest. Finally liquefaction and cyst formation may develop (Fig. 160). The cysts usually are small and multiple, the cyst walls ragged and lined with hyaline tissue. If the process becomes diffuse and extends up to the capsule, the wall may be smooth and fibrous. Uterine cysts are described on page 240. The hyaline changes do not advance beyond the capsule.

The transparent, glassy, hyaline substance does not give the microchemical reaction of amyloid. It is resistant to acids, and stains readily

with acid fuchsin (Van Gieson's stain) and eosin (Delafield and Prudden, 45). The substances are proteins and should not be confused with mucin, which is a glycoprotein and accepts basic stains. *Amyloid degeneration* in a gangrenous polyp has been described by Stratz (46).

Myxomatous degeneration is described by Gebhard (31) and Meyer (32). Its occurrence is denied by Frankl (24, page 58) and not mentioned by Lockyer (21, page 213). Very probably edema of a fibroid has been mistaken for this degeneration. Further research with use of special stains is required to settle the question.

FIG. 160.—CAVITY FORMATION IN UTERINE FIBROID—UNDERGOING HYALINE DEGENERATION. (×10.) The connective tissue mainly shows the hyaline degeneration. A central cavity has formed. 1. Cavity. 2. Wall of cavity composed of hyaline tissue. 3. Part of central hyaline content still in situ. 4. Intact muscle of fibroid with slight connective tissue changes.

FATTY CHANGES *(Infiltration, Degeneration)*.—This change is not frequent, and is usually limited to small areas of a growth. The color, on section is as yellow as that of fat. The markings of a myoma may disappear and the consistence become soft and pulpy. According to those who believe in fatty degeneration the protoplasm undergoes first granular, then hyaline and finally a fatty degeneration, which may result from necrosis or involutionary changes due to the puerperium (Martin, 47; Kleinhans, 48). Appearing late in the course of hyaline degeneration, butter-like contents of cysts, containing cholesterin crystals and fat droplets have been noted (Kelly and Cullen, 7, pages 92 and 124). Very probably fat

deposits from the blood stream, in consequence of altered circulation resulting during thrombosis and necrosis, account for a number of cases. So-called fibrolipoma or fibrolipomyoma, claimed not to be mixed tumors by some, have been reported by Jacobson (49) (developing in an atrophic myoma); Ley (50), Knox (51) (developing after the menopause), and Lockyer (31, page 225).

The process begins with the appearance of fat droplets within the protoplasm at the extremities of the nucleus (Gebhard, 31, page 110). Eventually these may completely fill the cell. Stained with Sudan III the fat globules may still show the course and direction of the replaced muscle fibers. Other degenerations, such as hyaline, may also be present. A true lipoma is lobulated (see page 260) but the exact classification of these growths is difficult. For description of the histology of lipolysis see Keiffer (52).

NECROSIS *(Red or Carneous Degeneration)*.—A slowly proceeding aseptic cell death (v. Franqué, 53) accompanied by hemolysis produces the peculiar appearance of carneous degeneration. But necrosis is encountered in all stages from cloudy swelling to complete disintegration.

The same gross circulatory changes mentioned under circulatory disturbances (p. 233) may be causative. The frequency of necrosis during pregnancy (Winter, 54), the preponderance of the hemolytic (carneous) type during gestation, and in the puerperium, bespeak the possibility of a toxic factor (Murray, 55).

The affected tumor in simple necrosis becomes puttylike and loses its elasticity and sheen. Later the tissue is dry and crumbly. The color depends largely upon the presence or absence of interstitial hemorrhage. In carneous degeneration Lockyer (21, page 227) mentions a peculiar fishy odor in addition to the raw or partly cooked beefsteaklike appearance.

According to Murray (55) the hemolysis of the blood corpuscles is due to lipoid substances derived from the muscle fibers. A certain amount of lipoid produces complete hemolysis, excess lipoid changes the color to brown, greater excess bleaches, while too little lipoid is insufficient to hemolyze so that the two latter quantities produce yellow to white necrosis.

The necrosis usually begins centrally, extending outward to the periphery. If very local, probably thrombotic, a central sequestration may result as figured by Frankl (24, page 58). Eventually, if complete disintegration has taken place, a cyst with dark grumous or dark liquid content may develop. Calcification in plaque or scattered form, in the latter case, often only microscopic in size, not infrequently marks the final changes.

The histological picture of necrosis is shown by a loss of tinctorial qualities of the cells, especially of the nucleus. Fatty infiltration is frequent. Gradually a faint, shadow-like substance still revealing the lumina of blood vessels as vacant areas, is all that can be perceived (Fig. 161). Microscopically, carneous cannot be distinguished from other degeneration. The periphery may shade off gradually toward a normal area in which the cell details become more and more visible and finally appear normal, or end abruptly at the capsule or in a definite line of demarcation.

3. **Inflammation.**—GANGRENE.—Infection of either a necrotic, or of an otherwise normal myoma may develop. Sitzenfrey (56) in thirteen cases of myoma complicated by fever found six to contain bacteria,

v. Franqué (57) likewise discovered bacteria. The infection can come from below, from the intestine, or be carried by the blood stream.

Rupture with consequent peritonitis (Drummond, 58), suppuration, abscess formation (Duvergy, 58a), abscess communicating with the gut, have all been reported. Kelly and Cullen report 11 cases with three deaths (7, page 153). Among them was an intraligamentous myoma containing 4.7 liters of pus and another with 10½ quarts of pus. Submucous myomata after infection from intra-uterine manipulation, or spontaneously in the puerperium, may become gangrenous and sloughing. They may produce pyemia or bacteremia (Vineberg, 59). Gas formation in a cyst is uncommon (Boldt, 60).

R. Meyer (61') has described a pseudomyoma due to localized metritis. This condition must be differentiated from an inflamed myoma.

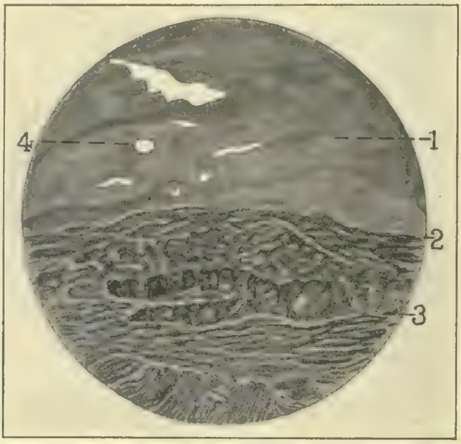

FIG. 161.—CARNEOUS FIBROID FIVE-WEEK POSTPARTUM. (Low power.) 1. Degenerated part of fibroid showing homogeneous tissue without structure. 2. Demarcation zone. 3. Musculature of arteries unaffected by degeneration. 4. Clear space left by lumen of blood vessel running through degenerated area.

CALCIFICATION AND OSSIFICATION.—Calcification takes place only in tissues of impaired vitality. It appears in microscopic amounts scattered in the connective tissue and in the muscle cells or may be found in plaques, varying from ½ mm. to 2 cm. in thickness (R. Meyer, 32, page 445), forming shells at the periphery of the growth.

Instances of complete calcification of fibroids—forming the so-called uterine stones, have repeatedly been observed (Everett, early lit., 62). Expulsion of the mass by rectum (Payr, 63), parasitic existence within the abdomen (Gil Wylie, 64), expulsion per vaginam (Thorn, 65), show some of the possible sequelae of complete calcification. Thorn's case and one reported by Kelly and Cullen (66) showed carcinoma of the corpus coincidentally. Ordinarily calcified myomata cause no symptoms. The nodules are noticed as stony, hard, yellow-white areas, projecting above the surface or arresting the knife when attempting to section the growth.

Calcified areas may be seen in the blood vessels of myomata and of the uterine muscle (Figs. 162 and 163). Ordinarily they are of no significance, appearing in comparatively young women and becoming increasingly numerous with repeated pregnancies and advancing years. Deposit of small

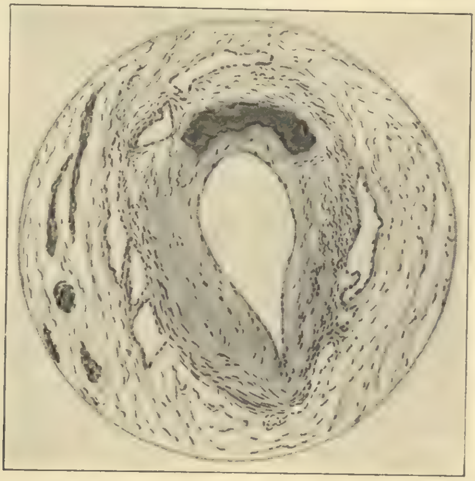

Fig. 162.—Calcification in a blood vessel of the uterus. (Medium power.) From a woman of 40 years who has borne children. In the media of the otherwise normal vessel is a semilunar plaque. This is of no significance pathologically.

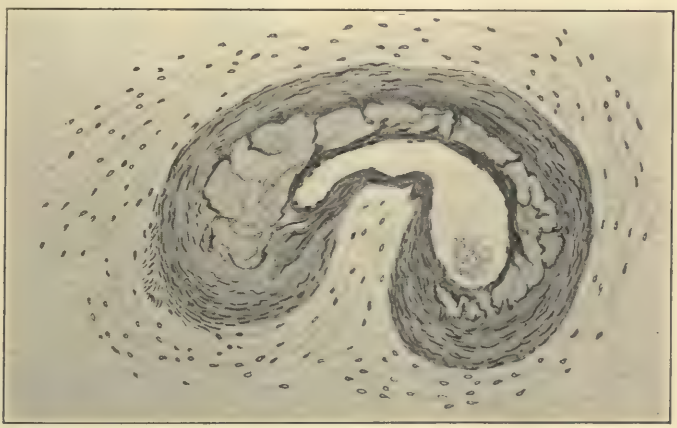

Fig. 163.—Oblique section of an artery in the uterus of a woman of 64 Years. (Medium power.) The arterio-sclerotic change in the media is due to senility. Spaces filled with detritus are noted. Later calcification may replace the lipoids occupying these cavities. The lumen of the vessel is unobstructed and contains red blood cells.

areas of calcium salts are frequent in myomata. The course of the muscle fibers may remain visible, or irregular homogeneous deposits, staining almost black with hematoxylin, are found within degenerated areas. Decalcification of the tissue is required before sectioning. Klotz (67) has

shown that after fatty degeneration, soap albumins are found within the cell and that these in turn unite with the calcium of the blood to form double calcium soaps. The final stage is a change into the insoluble calcium carbonate and phosphates.

Ossification is infrequent. It is always preceded by calcification and occurs within the calcified areas, Freund (68). Johnston's (69) case was reported incorrectly as an osteomyofibroma.

Cystic Myomata *(Pseudocysts)*.—Especially as a sequel to hyaline degeneration, more rarely following other types of degeneration such as necrosis, cystic spaces develop within fibroid tumors. Commonly multiple small areas liquefy, forming numerous cavities separated by trabeculae. With progression of the change, larger irregular cavities result from fusion of adjacent spaces. The walls are ragged. When the process finally halts at the capsule, the walls may become smooth as all the degenerated material is liquefied. If an entire fibroid necroses and is then liquefied, single, smooth-walled cavities may develop from the beginning.

Submucous myomata rarely undergo cystic degeneration. Interstitial and especially subserous tumors more commonly become cystic. Enormous tumors may develop (Lihotsky (70), cystic myoma containing 34 liters); Lingens (71), weight 45 pounds; Webster (72) 87 pounds; and Kelly and Cullen (7, page 512), 89 pounds. The uterine walls previously much thinned, may contract strongly after the tension exerted by the fluid is removed.

The fluid is most often straw colored. In small cysts it coagulates on exposure, if the liquefaction is due to hyaline degeneration. If necrosis precedes the liquefaction, the fluid is of chocolate color. In rarer instances cholesterin crystals and fat droplets are found.

Edematous areas, and small cystic areas due to lymphangiectases must be differentiated from pseudo cyst formation. Edema, under the microscope will be found intrafascicular, that is, separating the muscle bundles. Lymphangiectatic spaces are lined with endothelium.

Cysts due to dilatation of that part of Gärtner's duct coursing through the uterine wall are recognizable by their epithelial lining and submucosa (Combert, 73) and their position along the sides of the uterus.

Frankl (73a) describes a cyst within a cyst in the fundus uteri, both cavities being lined with cubical epithelium. He believes that the invagination of one uterine gland into another was the cause. The same author reports a cystic myoma lined with cubical epithelium with an excrescence on its wall showing *papillary carcinoma* (the possibility of an ovarian origin of the intraligamentous cyst is not entirely excluded.—R. T. F.).

Malignant Changes, including metastasising and vein myomata are preferably discussed under myosarcoma (p. 246).

Myoma and Pregnancy.—The influence of myomata on fertility, and that of sterility upon the incidence of myoma were discussed on page 227. In the presence of gross distortions of the uterine cavity, of menorrhagia and metrorrhagia, of marked endometrial hyperplasia, all due to the

presence of myomata, a serious hindrance to conception and nidation is evident without further explanation. However, even under these conditions gravidity may occur and proceed to term. In large series of obstetric cases, only from 0.45 per cent (Cragin, 74) to 0.6 per cent (Pinard, 75) of complications are noted.

In pregnancy purely mechanical interference may develop early if the myomata increase rapidly in size. Spontaneous abortion is not uncommon. The writer has had to remove the uterus, which filled the abdomen and produced excessive dyspnea from pressure, in the fourth and sixth months of pregnancy. Sometimes myomectomy is feasible.

During labor incarceration of a subserous myoma may block the pelvis. At times submucous myomata are expelled before the advancing head (Gordon, 76). Malpositions are frequent. Inertia and poor uterine contractions are often noted. The placenta, even after its detachment, may be retained above a projecting fibroid. Placenta accreta may prove a serious obstacle where the placenta has developed upon the atrophic mucous membrane covering a fibroid. Deep penetration of villi through a thin defective decidua devoid of spongy layer, into the muscle layers of the fibroid, occasion the adherence.

Post partum infection, sloughing and carneous changes in fibroids are unduly frequent. Ihm (77) has collected 57 fibroids showing such changes during pregnancy from the literature; post partum, the number is great The trauma suffered in labor, and varying degrees of infection of the uterine cavity during the puerperium, plus the abrupt changes in circulatory conditions account for this sudden incidence. A fibroid may mechanically block the escape of the lochia (Neubner, 78).

The diagnosis of myoma versus pregnancy may present difficulties even after the abdomen is opened. The writer recalls a case in which amenorrhea, a uterus of close to six months in size showing a typically gravid appearance and the presence of a large corpus luteum, induced him to advise reclosure of the abdomen. Six months later the now somewhat larger uterus, containing a solitary myoma was amputated. Under similar conditions he now performs an exploratory hysterotomy if the abdomen has been opened. Pomroy (79) has emphasized this difficulty as encountered in a tumor the size of a four months' pregnancy.

The increase in the size of the myomata during pregnancy is due mainly to edema. Hyperplasia of the individual muscle cells does, however, occur (Cornil, 80). The histology of carneous degeneration, necrosis and suppuration have been sufficiently discussed (vide ante).

In spite of what has been said, in a great number of cases fibroids complicating pregnancy produce no disturbances. In Cragin's series of eighty-nine cases, only eleven cases required special treatment in labor, and of these only four fibroids caused actual obstruction. Huge tumors may rise out of the pelvis during labor. Subperitoneal fibroids are most prone to cause trouble. The pregnant uterus is tolerant to operative interference

without the interruption of gestation (Frank, 81), permitting the removal of tumors which cause symptoms. Necrosis may cause peritonitic disturbances; infection produces true peritonitis.

For literature see Ohlshausen (82).

4. **Secondary and Coincident Changes in Endometrium, Tubes and Ovaries, etc.**—VASCULAR.—Sampson (83) studied the changes in the blood supply of the uterus by means of arterial and venous injection. A myoma has usually only one nutrient artery; the veins are very scant.

Small subserous myomata have no effect, large ones cause dilatation of the uterine vessels in the peripheral zone. Intramural growths are less vascular than the myometrium about them. In the submucous variety the veins over the tumor are often dilated. Cullen (l. c. 7, page 480) and also Frankl (24, page 54) found vessels running parallel to the surface, their caliber wide, often uniting into a network. The vessels under the surface epithelium may form veritable sinuses. Sampson (l. c. 83) found both menstrual and irregular bleeding in myomatous uteri due to venous sources. Only when sloughing of fibroids occurred was the blood arterial.

FIG. 164.—ATROPHIC UTERINE MUCOUS MEMBRANE OVER SUBMUCOUS FIBROID. (Medium power.) The mucosa is thin, the glands few, running parallel to the surface as do the thin-walled blood vessels. The surface epithelium is very low cuboidal (compression effect). Immediately below the thin layer of musculature shown at the bottom (but not appearing in the picture) is the capsule of the fibroid.

ENDOMETRIAL.—The writer has found the endometrium of myomatous uteri thick and hyperplastic, of the type of stationary hyperplasia, except when pressure produced atrophy or prevented such thickening. The mucosa responds fully to the cyclical influences. Signs of inflammation are usually absent.

The atrophy of the mucosa and parallel course of glands over the surface of a fibroid appears in Fig. 164. Hyperplasia of the endometrium occurs in the dead spaces between the growths. In areas relieved of pressure mucous polypi may be found in great numbers. The myometrium shows hyperplastic muscle changes as a result of fibroid growths which cause increased muscular (expulsive) contractions (submucous and intramural). The arterial and venous zone supplying the tumor or tumors is dilated.

Such secondary changes as *tuberculosis of the endometrium*—seven out of 1428 cases (Cullen, 7), one out of 400 (Frank, 8)—are purely accidental. Tuberculosis in a myoma is reported by Vassmer (84).

CANCER OF THE UTERUS may also be considered a coincidental occurrence, carcinoma appearing in 1.7 per cent of Cullen's 1400 cases (7), 2.4 per cent of Noble's (85) 1118. In the series of 400 cases of the writer, cancer was found twice, 0.5 per cent. Broun (85a), in 1500 cases, found malignant complications in 4.4 per cent.

McDonald (9) calls attention to the fact that in his series of 700 cases, adenocarcinoma occurred in 2.9 per cent (20 cases) and squamous-celled cervical carcinoma in only 0.8 per cent (6 cases). This means that three adenocarcinomata were found for every squamous-cell cancer, a reversal of the usual relation (100 squamous cell to seventeen adenocarcinomata). The same applies to Franz's statistics (86), for in 1390 cases there were seven corpus carcinomata to three of the collum. Whether this frequency is due to the fibroid growths, or is the result of a common etiological factor remains an open question. Very rarely *metastases of cancer* have developed within a fibroid. The original focus may be in the ovary (Bauereisen, 87), peritoneum (Davidsohn, 88), lung (Schopter, 89) breast (Pozzi, 90), etc.

TUBAL DISEASE occurs frequently in association with fibroids, either as an ascending infection (gonorrheal, septic), or hematogenous (tuberculosis). Kelly and Cullen (7) found gross changes in nine per cent of all tubes in 934 cases, McDonald (9) in 27.5 per cent of 700 cases, the writer in eighteen per cent of 400 cases. The following table shows the tubal complications noted in the writer's series.

Tubo-ovarian abscess	4
Tubercular salpingitis	3
Pyosalpinx	6
Hydrosalpinx	7
Chronic diseased adnexa	52

OVARIAN DISEASE is found in an unduly large number of fibroid harborers. This applies even if the so commonly found enlargement, microcystic changes, and overvascularity of the ovaries is regarded as functional. In the writer's series 13 per cent of ovaries showed such changes. Exactly six per cent showed serious ovarian disease—six papilliferous cysts, fifteen non-malignant cysts, three dermoid cysts. Kelly and Cullen (7) found ovarian adhesions in nearly fifty per cent of their large series. This, however, includes a large proportion of colored women.

OTHER DISTURBANCES.—The displacements upward of the bladder caused by subperitoneal cervical fibroids, or by large peritoneal growths; the compression and secondary dilatation of the ureters (Knox, 91), resulting from impacted pelvic fibroids, the opening up of the mesosigmoid and similar intestinal complications, all are noted as not infrequent sequels to myomata.

Vein Myoma.—Either growing into the vessel walls and carrying the

normal endothelial lining before them, or arising from the walls of vessels, a small group of intravascular myomata are found. Knauer (92) reported four cases growing as strandlike white masses in the vessels of the broad ligament and uterine wall. The strands consisted of unstriped muscle, in parts undergoing hyaline degeneration, covered with intima and endothelium. In Dürk's (93) case a columnlike tumor extended from the stump of the hypogastric artery, through the vena cava, into the auricle. Sitzenfrey (94) reports three cases. In one he pulled a strand 8 cm. long from the distal end of the uterine vein. The patient reported as well 1½ years after operation. Schneider (95) has reported a case.

The writer, after having studied the section submitted to him through the kindness of Dr. Ries, regards the case described by that author (96) under the title of villi persisting for eighteen years, as a case of vein myoma. These tumors are most often sarcomata. Like other growths which reach the vascular system, they assume branching, strandlike form.

Grapelike Myoma has been described by Mandl (97). Innumerable small grapelike globules arising from a vascular pedicle project either submucously or subserously. The mechanical or other reasons which produce this rare type are unknown.

"Benign" Myomata with Metastases appear so doubtful that they will be discussed under sarcoma.

Myoma developing after Castration or after the Onset of the Menopause.—Fibroids not only can continue to grow after the onset of menopause, but may even begin to develop after the onset of the physiological or operative climax. Gibson (98) observed the appearance and growth to the size of a child's head of a fibroid within seven months of castration. Müller (99) and Müller and Kottmann (0.9 per cent beginning after the onset of climax), Johnson (100) also Hofmeier (101) discuss fibroids developing after onset of the menopause. Leo (102) reported a submucous fibroid twelve pounds in weight which sloughed thirty-two years after castration. Myomata have also appeared in the stump remaining after supravaginal hysterectomy, Doleris (103), Küstner (104).

II. SARCOMA OF THE UTERUS

Etiology.—FREQUENCY.—Compared to epithelial tumors, sarcoma of the uterus is a rare disease. For every sarcoma there are from thirty to forty carcinomata. Evans (105), using the material of the Mayo clinic, found the proportion, 1 : 40 (22 to 873). Veit (106) in 42,395 gynecological cases found 1493 carcinomata to 40 sarcomata (1 : 37.2).

Evans found 72 malignant myomata in 4000 cases operated upon for uterine fibroids (1.8 per cent); Geist (107) in 540 cases of myoma found 22 sarcomata (4.07 per cent); the older statistics of Miller, Lewis and Olshausen (see Geist, 108) comprising more than 17,000 cases of fibroids

showed 1.3 to 1.9 per cent due, doubtless to the fact that only suspicious-looking tumors were examined microscopically. Kelly and Cullen (7, page 170) in 1400 fibroids found 17 sarcomas or 1.2 per cent. Warner (109) in a small series found 7 per cent of cellular fibroids, but only 2 per cent of positive sarcomata. Fehim (110) continuing Warnekros' series at Bumm's clinic reports the unduly high number of 74 sarcomata in 580 cases or 12.8 per cent. Frantz (111), likewise reporting Berlin material, found only 0.64 per cent (1390 fibroids, 9 sarcomata).

Evidently there are great differences in interpretation of the histological findings in early or suspicious cases. Some authors include "cellular fibroids" (Fig. 165) among the sarcomata, others bar all but very positive

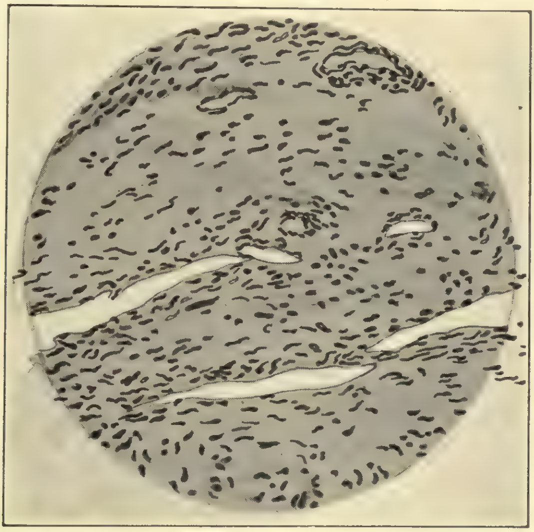

FIG. 165.—CELLULAR FIBROID OF UTERUS. (Medium power.) Non-malignant, as in spite of cellularity the nuclei are regular in size, shape and chromatin content.

new growths. Thus only can the great difference in percentage be accounted for.

AGE.—Veit (106, page 519), in a collection of 438 cases, found a few cases in early life, mainly arising from the mucosa (v. d. Hoeven, 112, child nine-months old), with a rapid increase from the 25th year up. The greatest number appear between the ages of 45 and 50. From there on there is a sharp decline. Sarcoma uteri is a disease of the climacteric. About 25 per cent of the patients were nulliparous.

SITE.—Corporeal sarcoma is more common than cervical (Piquand, (113), 393 to 68; Gessner (114), 8 to 1; Meyer (115), 29 to 1).

Using the old nomenclature introduced by Virchow, mural sarcoma is more frequent than sarcoma of the mucous membrane (Schottländer, 116, 40: 7), but as a tumor progresses its exact primary location can no longer be determined. Piquand (113) contrasting intramural, submucous and

subserous origins, found them as 60: 63: 45, Kelly and Cullen (l. c., 7, page 171) as 9: 3: 5.

TYPES.—Sarcoma appears either as a circumscribed nodular tumor (independently, or within a fibromyoma) with more or less well defined margin toward the musculature, or as a diffuse growth.

Circumscribed growths are most often intramural but readily extend inward toward the uterine cavity, in which case they become polypoid, or outward to the peritoneum, which they may penetrate and upon which they may then spread rapidly. When developing in a fibroid an outer shell of myomatous tissue is found as evidence of such origin. However, during the further course of the disease, this shell may be perforated or entirely destroyed. At times a sarcomatous nodule may appear sharply demarcated and encapsulated; usually even then the microscope will show infiltration beyond the capsule tissues (Figs. 175 and 176, p. 255).

Diffuse Growths are usually submucous. Diffuse intramural growths are extremely rare. Ordinarily submucous tumors involve the entire uterine cavity (33 of 54, Piquand, 113). Polypi are the rule. The uterine cavity is dilated and filled with closely packed polypoid and sessile masses. Intracervical growths or portio tumors may appear in cauliflower, ulcerating or grapelike form or as diffuse enlargements of the entire cervix. The so-called sarcoma botryoides is a true mixed tumor and will be described separately (p. 261).

The *"recurrent fibroids"* of older authors were doubtless polypoid sarcomata. Since the histology of sarcoma has become better known a few similar cases are recorded. Croom (117) six times removed huge masses from below. Each time the material proved to be "edematous fibroids." After two years a hysterectomy showed sacroma. Kelly and Cullen (7, page 179) record a case where myomata were expelled three times in succession.

MACROSCOPIC APPEARANCE.—The gross appearance of sarcomatous tissue, if the sarcomatous changes are well marked, differs both from that of the normal musculature of the uterus and from the appearance of fibromyomata. In the early stages no macroscopic changes may be determined. For example while Winter (118) examined only those fibroid growths which appeared suspicious, his percentage of sarcomata was 3.2 per cent, when every tumor was submitted to examination the percentage rose to 4.3 per cent.

The more the tumor tissue differs from uterine musculature in its histology the more puttylike and homogeneous do the growths show on section. The color is white to gray to yellow, lack luster and devoid of tendinous sheen. Various degrees of hemorrhage appear as red to blackish areas. Cysts, which may attain large size, softened foci, or myxomatous regions may impart a variegated look to the mass. The surface of submucous or polypoid growths are often smooth. Where the tumor has broken through the mucosa or serosa it may have a pulpy, brain-like appearance and is friable. On the other hand both sarcomatous polypi and fibro-

mata may macroscopically seem non-malignant. Usually some lack of marking and sheen or the presence of a slight tinge of yellow, some opaqueness, dryness and friability arouse suspicion. The mucosa may persist in far advanced sarcoma. Rarely it is totally destroyed or substituted by granulation tissue (pyometra) (Williams, 119).

The size of sarcomata is variable. Small foci within a fibroid may be the sole evidence of malignant disease. The foci may be multiple (Busse, 120). Huge tumors have been described by Terillon (121), 20 kg.

Just as in non-malignant growths the uterine muscle may hypertrophy. This applies especially to sarcoma developing in a fibroid and to intracorporeal growths developing slowly.

EXTENSION.—Sarcomata after penetrating the peritoneal coat may extend through the abdominal wall and perforate the skin. Intestinal fistulae may develop, the peritoneum may be involved or septic peritonitis set in (Finley, 122). Infiltration of the parametria is common. Intraligamentous growths may be due to development within a preëxisting intraligamentous fibroid or to extension beyond the uterine wall. The growth may extend along the fallopian tube or involve the ovaries (Peine. 123). Cervical sarcoma eventually involves the vagina.

RECURRENCE after extirpation occurs rarely in sarcomata found in the center of myomata. The more unripe forms recur most frequently. Local *recurrences in the cervical stump* are on record (Hansen, 124, Fehim, 110). Where the parametria are involved or retroperitoneal glands are affected extirpation can, of course, not affect the outcome.

METASTASES are commonest through the blood channels, hence pulmonary growths are most often found. Next in frequency, liver, intestine, omentum, kidney and bone are involved. Rarely the so-called malignant myoma may produce multiple metastases (Krische, 125). The ovaries (Kaufmann, 125a) and the retroperitoneal lymph glands may be involved.

The structure of the metastases commonly does not differ from that of the primary growth. At times more marked polymorphism or a preponderance of one type of cell has been noted.

MICROSCOPIC APPEARANCE.—All transitions from the non-malignant fibromyoma, through the ripe types of "myosarcoma" down to unripe, small, round-celled (lympho) (Wagner, 126) sarcomata can be traced. These purely morphological resemblances cannot be used as argument in favor of histogenetic relationships (R. Meyer, 115). The malignant degeneration of the older authors and direct transitions from normal muscle fibers to tumor tissue at the periphery as described by Gebhard (127), Williams (119), Cullen (7), etc., are no longer interpreted as evidence of a change of the normal tissues into sarcoma.

Myoma Malignum (sarcoma myomatoides or myocellulare) is true sarcoma which in gross and microscopic appearance closely resembles myoma but which shows an infiltrative growth and metastases.

The histology of the tumor, as R. Meyer (128) justly says, always

differs from that of simple fibromyoma. There is less connective tissue, the cells shows various atypical nuclear changes (more or less chromatin), mitoses and amitoses. Careful examination shows the presence of other types of cells—spindle, round or giant cells.

Meyer regards the appearance of these atypical characteristics as a cell degeneration—as the evidence of sarcomatous characters previously present but invisible. However, myoglia fibrils may be found as in the case described by Mallory. For literature covering the growths see Mallory (1), Ribbert (129), R. Meyer (128).

Muscle-cell sarcoma or "myosarcoma" are less fully differentiated growths than the above. They may contain a variable number of muscle elements intermingled with other types of cells. A sharp distinction should

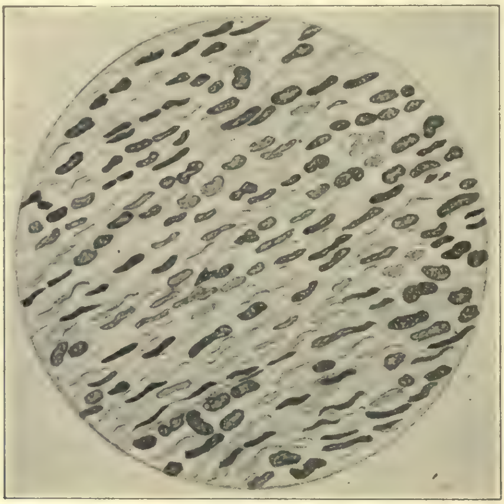

FIG. 166.—MYOSARCOMA OF THE UTERUS. (Medium power.) Note variation in cell type and the appearance of "activity" distinguishing it from a cellular fibroid. (See Fig. 165.) The nuclei vary in size, shape and chromatin content. In some parts of the tumor not shown, the spindle-cell type predominates.

be drawn between preformed muscle elements remaining within an invasive growth (Fig. 166).

The difference in chromatin content, variability in size and shape of nucleus, thickening and shortening of cell body, extreme cellularity and general appearance of "unrest" become more marked as unripe growths are examined. According to Evans (105), the number of mitoses encountered is an exact index of the clinical malignancy. Invasive and infiltrative growth can be distinguished at the periphery where areas of tumor cells are found beyond the capsule (if in a preformed myoma). Hyaline degeneration of the intercellular tissue occurs frequently and early.

Spindle-cell sarcomata usually do not occur as pure types, but either

approach the muscle-cell or round-cell forms. The spindle cells are smaller and slenderer than the muscle cell. The nucleus is oval, shows marked

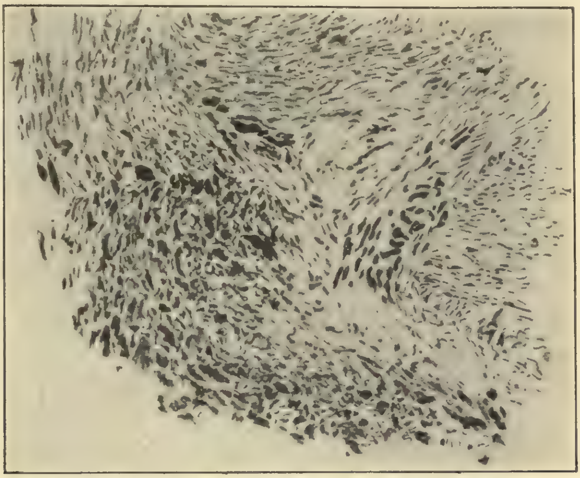

FIG. 167.—SARCOMATOUS CHANGE IN A UTERINE FIBROID. (Medium power.) The upper right hand areas show but slight variation from a normal fibromyoma. The lower left hand shows typical, somewhat polymorphic spindle cell sarcoma.

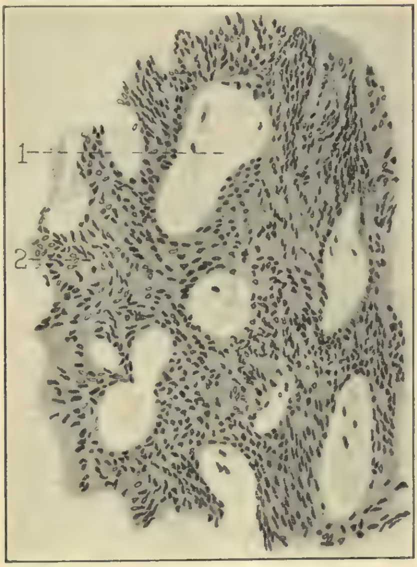

FIG. 168.—SPINDLE-CELL SARCOMA OF CERVIX WITH HYALINE DEGENERATION. (Medium power.) The entire picture is that of "unrest." Note the irregular course and distribution of the cells, with considerable irregularity in the size of the nuclei. 1. Hyaline area of degeneration. 2. Sarcoma cells.

variation in chromatin content. The cell body may be long and slender or plump (Fig. 167). The intercellular substance is scant (Fig. 168).

This tumor must be differentiated from the infiltration of subacute metritis (R. Meyer, 115, page 470).

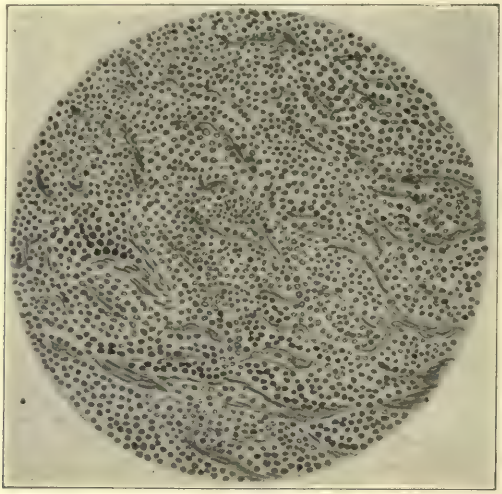

FIG. 169.—SMALL ROUND-CELL SARCOMA DEVELOPING IN AN INTRALIGAMENTOUS FIBROID. (Medium power.) The small round cells are seen separating the still intact muscle fibers of the fibromyoma. A diffusely staining stroma gives an indistinct appearance to the section.

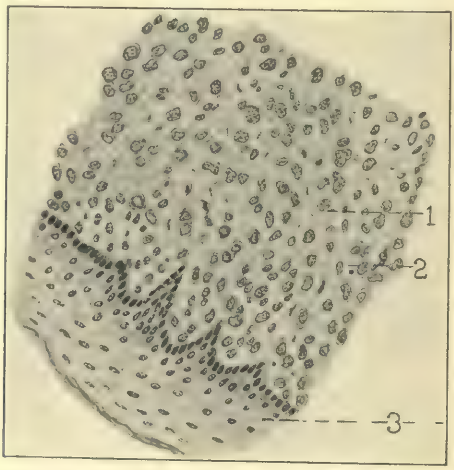

FIG. 170.—LARGE ROUND-CELL SARCOMA OF CERVIX. (High power.) The tumor is seen beneath the intact surface epithelium of the portio. The intimate relationship of the tumor cells to the connective tissue substrat is shown and clearly differentiates this growth from a carcinoma, to which it bears a superficial resemblance. 1. Sarcoma cell. 2. Connective tissue. 3. Surface epithelium of cervix.

The round-cell sarcoma even more rarely is pure in type; muscle, spindle and giant cells can usually be demonstrated in some part of the tumor. Tumors composed of small round cells which are very rare, resembling the

lymphosarcoma (Fig. 169), and large round cell growths are recognized (Fig. 170). The latter may be alveolar in type (to be distinguished from a pseudo-alveolar distribution due to infiltration of preformed septa as in cervix) and is then difficult to differentiate from carcinoma (Fig. 171). These round-celled sarcomata have been confused with endothelioma when arising in the cervix. Cross-section of muscle bundles or of spindle cells may also give the appearance of round cells.

As is to be expected from the more unripe state, the deficiency of intercellular substance and the preponderance of cellular elements, these tumors readily undergo degenerations, necrose and show hemorrhagic foci. They also metastasize early.

The small round cells are from 4 to 6 micra in size, mainly composed of nucleus, the cell outline being ill defined. The large round cell is not

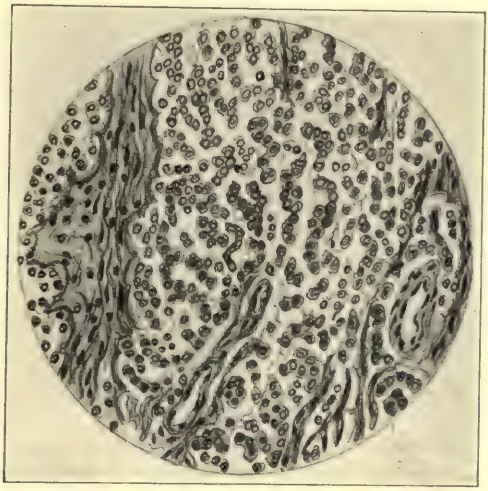

FIG. 171.—LARGE ROUND-CELL SARCOMA OF UTERUS. (Medium power.) The tumor shows a sharply demarcated capsule. The portion here illustrated has an alveolar arrangement due to the connective tissue septa separating the masses of sarcoma cells.

above 15μ, of which the nucleus occupies 8 to 12μ. The nuclei accept the stain irregularly. Mitoses are small (Gebhard, 127).

Giant-cell sarcomata are usually found in polymorphous growths. The giant cells have not the peripheral type of nuclei but central, bizarre forms. The cell complexes may show the sheetlike symplasmatic appearance found in all rapidly growing unripe tissues (as syncytium, carcinoma, etc.). The intercellular substance may be well develop, Fig. 172 showing a giant-celled fibrosarcoma of the uterine wall occurring in polypoid form.

The giant cells, according to Gebhard (127), may reach 80μ in length. Their cell body shows diffuse affinity for basic stains. For literature see Moraller (130).

The *frequency of occurrence of the different types* is given by Piquand

(113) as spindle, 42; polymorphous, 34; round celled, 26; Geist (107), 11:9:2.

Evans' figures arranged according to the same classification are 33, 22 and 6. The spindle-cell type evidently predominates, polymorphous forms being a close second.

Secondary changes in sarcomata resemble those found in myomata and have been described with such detail in that connection (p. 233) that only cursory reference is here necessary. The more ripe the cell (muscle and spindle) the less marked and widespread are the degenerations. In unripe forms—round-cell, mixed, giant-cell tumors, more degenerative changes are encountered. Through overhasty growth, vessel changes, infection,

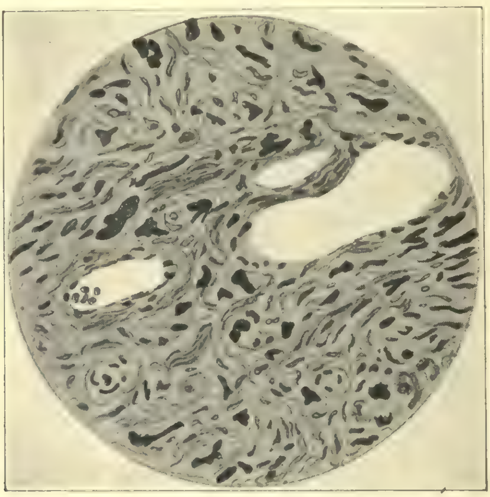

FIG. 172.—FIBROSARCOMA OF THE UTERINE WALL—POLYPOID. (High power.) The coarse fibrous stroma predominates over the large irregularly nucleated cells of the sarcoma. There are numerous capillaries.

etc., necrosis, fatty degeneration, sloughing, liquefaction and cyst formation are produced. Often only a peripheral shell of intact tumor tissue remains.

Cystosarcoma is due to massive necrosis in sarcomata. Small multiple cyst formation resulting from lymphangiectases have been described (Menge, 131) and can be recognized by their endothelial lining. The large cysts resemble those seen in fibroids. Piquand (l. c. 113) has collected 20 cases.

Special Types of Sarcoma.—Alveolar arrangement has previously been referred to. Occasionally it is dependent on preformed septa or connective tissue strands. R. Meyer (115) describes tumors with radiating, large and small alveolar structure. Fig. 173 demonstrates the types of these growths and their morphological similarity to carcinoma.

Angiosarcoma most often results from the persistence of cells around blood vessels because of better nutritional conditions. Fig. 174 portrays

such a growth, being the retroperitoneal metastasis of a polymorphous uterine sarcoma which showed no such perivascular characteristics.

Perithelial (Gottschalk, 132) and cylindromatous tumors are likewise to be considered as accidental vagaries resulting from nutritional conditions.

Melanosarcomata of the uterus have been described. Most of the cases are doubtful, being due to blood imbibition. J. W. Williams (119) described a case with brain metastasis.

Schlagenhaufer (132a) reports a case of *lymphosarcoma* of the uterus and adnexa as part of a general lymphosarcomatosis. The tissue was com-

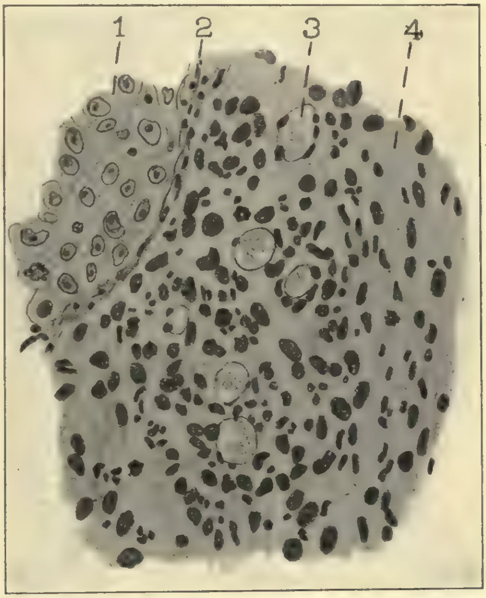

FIG. 173.—POLYMORPHOUS CELL SARCOMA OF CERVIX. (Medium power.) This sarcoma was difficult to distinguish from a carcinoma. 1. Alveolar distribution of cells resembling epithetial cells. 2. Connective tissue septum. 3. Capillary vessels. 4. Typical sarcomatous tissue.

posed of lymphocytic cells in a reticular stroma. He accepts only Wagner's case as authentic.

HISTOGENESIS.—The metaplasia of muscle into spindle and other types of unripe sarcoma cells was formerly accepted without reserve (Gebhard (127), Williams (119, 133), Cullen, 7). Infiltrative and degenerative changes at the periphery of tumors were interpreted as transition stages.

Since then Lubarsch, R. Meyer (135) and others have denied such metaplastic changes. Presumably an indifferent "anlage" may form a myoma, or a sarcoma, or part of the unused germ may develop within a myoma to form a sarcoma (R. Meyer, 135). The same author implies that an unripe type (round or polymorphous cell) may later develop into a riper spindle or muscle cell form. He considers perivascular, angio or lymphangiomatous distribution as of accidental origin and of no histogenetic sig-

nificance. The sarcomata of the mucosa are supposed to develop from the deeper layers of this membrane. These hypotheses are purely speculative.

Differential Diagnosis.—On *gross section,* macroscopically appearing lack of luster, absence of marking and puttylike consistence is of aid when well developed. In the majority of instances the microscope alone will show infiltrative growth, macroscopically no extension beyond the capsule may show (Figs. 175 and 176). *Sections of tumors* show marked differences in chromatin content of nuclei, variations in nuclear size, mitoses, polymorphism. As Kaufmann (136) emphasizes, diagnosis of endometrial sarcoma from curetted material may prove difficult. Exact orientation of the layers of endometrium and recognition of the menstrual stage by means of the low

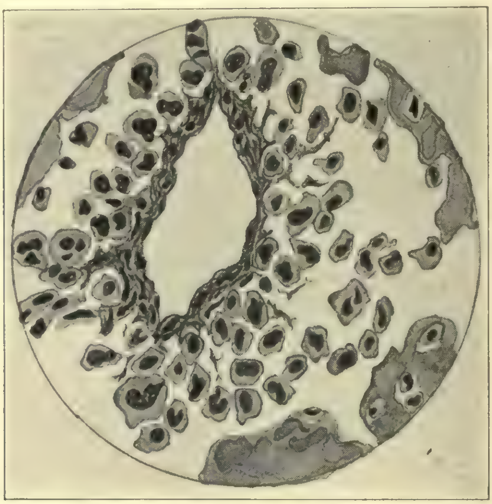

FIG. 174.—POLYMORPHOUS CELL SARCOMA OF UTERUS WITH PERIVASCULAR DISTRIBUTION AND WIDESPREAD NECROSIS. (High power.) Centrally is a small blood vessel surrounded by a radiating mantle of sarcoma cells. Along the periphery are areas of degenerating tumor cells.

power is essential. Only then can infiltration by unevenly staining strands of round or spindle cells, destruction and overgrowth of uterine glands and absence of surface epithelium be determined surely (Fig. 177).

Clinically sarcoma of the uterus is a treacherous disease. Most often neither symptoms or physical examination are of positive value except, in accessible cervical growths or in corporeal tumors, in the latest stages when periuterine infiltration, ascites and metastases may appear. Sudden increase in growth rate of a preëxisting fibroid is suspicious. Likewise the presence of anemia or cachexia not accounted for by loss of blood due to a fibroid. The repeated recurrence of submucous "fibroids" has been referred to. Intraperitoneal hemorrhage from a breaking down subserous tumor

(Fabricius, 137), inversion of the uterus (Williams, 138), etc., too closely resemble similar accidents noted in fibromyomata to be distinctive.

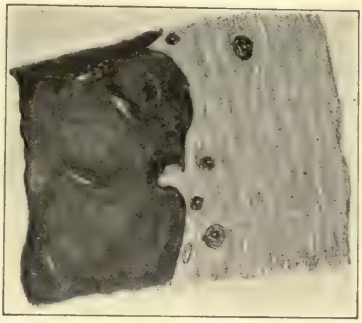

FIG. 175.—SARCOMATOUS UTERINE FIBROID (×3). Apparent encapsulation of the growth Dark portion is sarcoma.

POSTOPERATIVE RESULTS.—The permanent cures obtained after operation according to Veit (106, p. 542) are no better than those resulting after radical operation for cancer. The statistics are scant and incomplete.

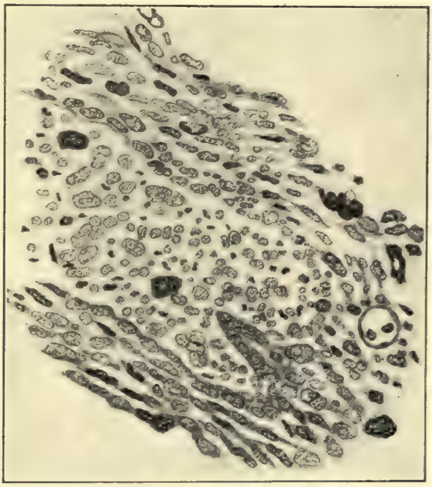

FIG. 176.—SARCOMATOUS FIBROID. (High power of Fig. 175.) Marked polymorphism, giant cells. Arrangement in pseudo-alveolar form.

Stump recurrences after supravaginal amputation of the cervix for supposed fibromyoma is not very uncommon. Reëxamination of the primary "fibroid," if available, usually shows sarcoma, which was overlooked (Spencer, 141). Malignant changes are frequent after the menopause. Fehling (142), Fehim (l. c. 110.)

III. ENDOTHELIOMA OF UTERUS

Endothelioma is progressively becoming a rarer tumor as cases are more carefully catalogued under other types. Nevertheless tumors arising from the endothelium—capillary, lymphatic and perithelial, or from serous surfaces—may occur and as R. Meyer (143) emphasizes, may be either benign or malignant. Hypothetically the benign types will resemble spindle-cell fibromata or adenomata, depending upon whether the connective tissue or epithelial characters of the endothelial cell predominate (benign proliferation of lymph vessel endothelium, R. Meyer, 144).

Dorland (145), without too sharp a critique, has collected 50 cases of endothelial tumors of the uterus of which 18 show "peritheliomatous" and 32 endotheliomatous types. The average age was 46 years—the youngest 18 years, the oldest, 68 years. Of 30 endotheliomata 16 were cervical, 14 corporeal. In 44 cases, where recorded, 19 were associated with myoma.

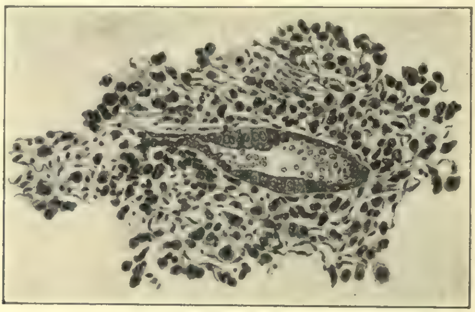

FIG. 177.—POLYMORPHOUS-CELL SARCOMA OF THE UTERINE MUCOSA. (High power.) Centrally a still intact uterine gland is shown completely surrounded by the tumor tissue.

The malignancy is relatively low (Bayon, 146). More carefully applied histological criteria would doubtless place many of the recorded cases among vascular tumors of the angiosarcomatous type, embryonal epithelioma and atypical forms of ordinary epithelioma of the cervix (Ewing, 148). Johnstone (147) and Shaw (147a) review the English literature.

MICROSCOPICAL.—The criteria given by the authors—which include transitions from endothelial to tumor cells (Fig 178), distribution in strands or network (Fig. 179), particular morphology of cells (Fig. 180) are not decisive. Lymphatic extension of cancer and even lymphatic proliferation due to cervical inflammation produce similar pictures. According to R. Meyer (115) the presence of sarcomatous and adenomatous tissue arising from the same cell material (?) or a tumor showing neither clearly carcinomatous or sarcomatous type should be classed as endothelioma.

The tumors illustrated in the text conform in morphology with endothelioma as usually described. The types shown include the solid (Fig. 181) and tubular (Fig. 178). The writer is unwilling to hazard a guess as

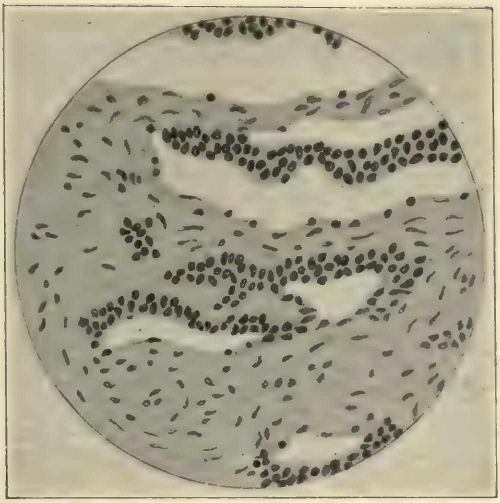

Fig. 178.—Endothelioma of uterus. (Medium power.) Mantles of endothelial-like cells lining, usually on one side, otherwise normal lymph vessels. Small groups of these cells are also found scattered in the stroma without contact with lymphatics.

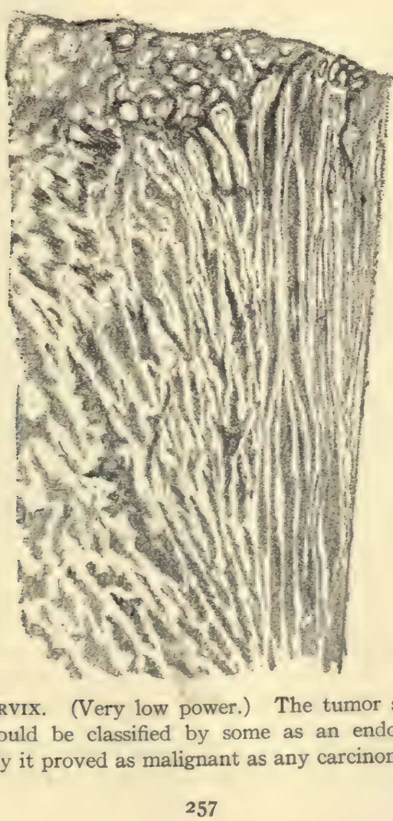

Fig. 179.—Tumor of cervix. (Very low power.) The tumor shows endothelial distribution. The tumor would be classified by some as an endothelioma, by others as a carcinoma. Clinically it proved as malignant as any carcinoma.

to their histogenesis, particularly as they are unaccompanied by clinical or other data (old specimens from the pathological collection of the College of Physicians and Surgeons, Columbia University, acquired during the professorship of Dr. T. M. Prudden).

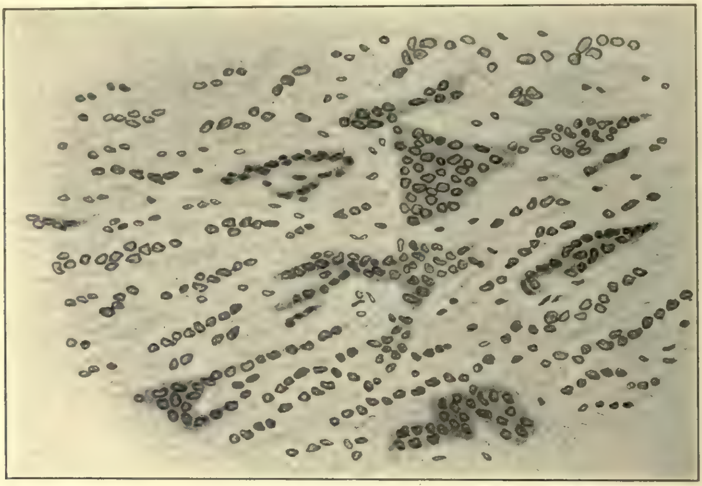

FIG. 180.—ENDOTHELIALLY DISTRIBUTED TUMOR OF CERVIX. (Medium power.) The tumor consists of small groups of cells with darkly staining protoplasm and clear nucleus, distributed in small groups and narrow columns within the tissue or lymph spaces.

FIG. 181.—ENDOTHELIOMA (?) OF UTERUS. (Medium power.) Throughout the specimen the distribution of cells is similar to the portion illustrated. At " 1 " is a lymph vessel from which some of the cells appear to originate.

Carcinosarcoma.—Carcinoma and sarcoma have been found existing separately within the same uterus (Montgomery, 149, Spencer, 150, Schmorl, 151). Hertel (152) found carcinoma of the cervix in 8 cases of

29 cases of uterine sarcoma. The recent literature will be found in Outerbridge (153). It is readily seen that intermingling of the two elements may later occur. v. Hansemann (154) believes that the stroma of a cancer becomes sarcomatous, Virchow that carcinoma and sarcoma arise like two branches from the same stem. Frequently the two types are found at the base of a sarcomatous polyp (Findley, 154a). It is usually impossible to decide which growth is primary.

Histologically adenocarcinoma and giant cell sarcoma are most often noted in conjunction. Meyer (115) describes an "adenoma malignum" combined with a polymorphous spindle cell sarcoma (polypoid). Frankl (155) reports a similar case, the sarcomatous polyp being "enormous."

In Albrecht's case (156) a polypoid sarcoma of the uterus caused inversion of the organ and carcinoma developed in the mucosa. Rosenstein's (157) case occurred in a child two years old.

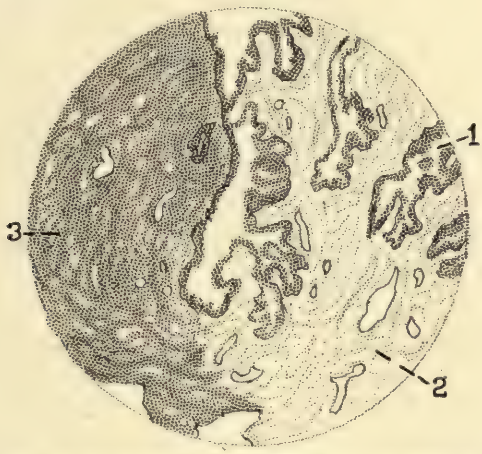

FIG. 182.—ADENOSARCOMA (?) OF UTERUS. (Very low power.) The section shows the junction of typical adenocarcinoma with a polymorphic cell sarcoma. In other portions, the two types are found intermingled. 1. Adenocarcinoma showing glandular type. 2. Normal uterine tissue. 3. Polymorphous sarcoma.

Diffusely growing carcinoma, atypical cell proliferation in polypi and inflammatory changes in the stroma of polypi must be ruled out before a diagnosis of carcinosarcoma is justified. Figs. 182 and 183 show what the writer interprets as an accidental mingling of adenocarcinoma and polymorphous cell sarcoma. It is impossible to determine which growth was the primary one.

The metastases most often show either carcinoma or sarcoma alone. In Kubinyi's (158) case the bone metastases were sarcomatous, those of the soft parts carcinomatous.

IV. MIXED TUMORS OF THE UTERUS

These tumors are mesodermal in origin. They are of rare occurrence. Two types are recognized, simple heterologous tumors such as lipoma of uterus, and complex tumors such as rhabdomyxochondroma. Unlike the mixed tumors of the vagina, which are commonest in infancy, these uterine growths are most frequent in the late decades. Except for lipoma, which appears oftenest in the fundus of the uterus or in the tubal angles (Ellis, 158a, 10 corporeal to 4 cervical) mixed tumors are found mainly in the cervix. At most, 10 have been reported in the corpus (Kehrer, 159, Herb, 160).

FIG. 183.—ADENOSARCOMA (?) OF UTERUS. (High power of Fig. 182.) 1. Indistinct gland with epithelium showing many mitoses. 2. Polymorphous sarcoma tissue intermingling without sharp demarcation with the glandular structures.

Lipoma is either simple lipoma, lipomyoma, lipofibromyoma or liposarcoma. Veit (106, p. 572) tabulates 17 cases of which at least two are probably due to fatty degeneration of myomata and are not lobulated, true tumors. Sitzenfrey (161) reported a liposarcoma. Kelly and Cullen had one case (Knox, 162), and two tumors with small quantities of fat interspersed. Ley's (163) case may be of the same character. R. Meyer (128) reports coincidental occurrence of an intramural lipomyosarcoma and polypoid adenoliposarcoma in the same uterus. For literature see Seydel (164), Elkin and Haythorn (165). Two cases were polypoid, the others were sessile corporeal growths.

R. Meyer derives the fat tissue from indifferent "lipoblasts," small round cells from which transitions to the fully developed fat cells can be traced. Connective-tissue cells, fibrilles and muscle cells are found. Com-

binations with sarcoma are frequent. Degenerations of various kinds are noted.

Chondroma and *osteoma* are still rarer. Meyer mentions only one case, that of Feuchtwanger (166), in which small to large particles of cartilage and bone appeared within a myoma. The surrounding tissues were well preserved and showed no degenerative changes or lime deposits. The more complicated tumors will be described presently. In these the presence of cartilage is common.

Rhabdomyoma, myxoma — striped muscle — has been found in the uterus without tumor formation (see p. 85). When appearing in tumors these are usually complex, mixed growths also containing glands and cartilage. For literature see Glynn and Bell (167).

Myxomatous tissue may be of embryonal origin (Siedamkrotzky, 168 showing spindle or branched cells, or result from degeneration. The determination as to mode of origin may be impossible.

Complex Heterologous Tumors.—In 1908 only 11 cases originating in the corpus uteri had been described, R. Meyer (106). The remainder were tumors of the cervix. Occasionally diffuse cervical growths have been found (Pick, 169), which infiltrate the parametria. Local enlargement of the cervix may develop; by far the greater majority are grapelike sarcoma (sarcoma botryoides).

The grapelike form is a secondary, unessential quality, as is proved in cases where the original growth is of small polypoid form, but the recurrence is botryoid (Pfannenstiel, 170). Not all botryoid sarcomas are complex or even simple mixed tumors. *Grapelike sarcoma* of the uterine body also occurs (Keitler, 171). The grapelike mass usually protrudes from the external os, may involve the portio and distends the vagina, in many ways macroscopically resembling an hydated mole. The grapes may be grayish-white, clear and translucent, or dark if hemorrhage has taken place. The stem is firm and fibroid, the nodules soft and edematous. Infiltration of the vicinity, near by metastases by blood and lymph channels, and rarely distant metastases render the tumor very malignant. No permanent cures are on record. Metastases may show the complex nature of the primary growth (Kunert, 172), or, originating from an apparently simple sarcoma, develop this complexity (Bäcker and Minnich, 173).

Histologically the mixed tumors consist of a diffuse indifferent cytogenic round-celled ground issue (Pfannenstiel, 170; Wilms, 174), representing the mother substance from which spindle cells, striped and unstriped muscle, cartilage, bone (Kehrer, 159), fat and myxoma tissue differentiates. The malignant parts usually are typically sarcomatous (spindle, round, polymorphous or giant cell) but occasionally approach the carcinomatous type, the middle position between connective tissue and epithelial form being characteristic of mixed tumors.

For the literature of rhabdomyosarcoma see Glynn and Blair Bell (167) —20 cases, of which 14 ended fatally. Pfannenstiel (170), Kehrer (159),

Seydel (164), Wilms (174), cover the fundamental literature. Epithelial and glandular inclusions, probably derived from the uterine mucosa, are described by Thiede (175), Penkert (159), adenocarcinoma, Murray and Littler (159a), adenochondrosarcoma, and others.

Fig. 184 shows a mixed tumor of the corpus uteri in a woman of 70 years. The specimen was removed by the curette. The patient died shortly after from metastases, no autopsy. Carcinomatous glands, squamous surface epithelium and striped muscle fibers appear in the section. Case of Dr. Eli Moschcowitz.

FIG. 184.—MIXED TUMOR OF THE UTERUS (CURETTINGS). (High power.) From a woman of 70 years who died with multiple metastases. In the center is a carcinomatous gland, to the left, is embryonal striped muscle, to the right the uterine surface epithelium is seen transformed into the squamous variety. (Specimen of Dr. Eli Moschcowitz.)

Histogenetically these tumors are of great interest. To account for the presence of the heterologous tissues various theories have been enunciated. The first theories explained the origin of the tissues by metaplastic changes from fibrous or muscle tissue (Pfannenstiel, 170), by metaplasia from the unripe sarcoma tissue, which was supposed to differentiate into muscle fat, cartilage, bone, etc. Metaplastic changes do occur but they are degenerative (as calcification and bone formation) and never progressive so as to produce tumors.

Complex tumors are most readily explained by means of Wilm's theory (174) of a displaced embryonal germ. The indifferent germ must be a

mesodermal cell in order to supply both the myotom (striped muscle) and mesenchymal (cartilage, etc.) derivatives. The indifferent tissue appears as a myxomatous or round-cell ground substance. Meyer (176) agrees with Wilms except that he does not believe that the wolffian duct pushes down the cell germ ahead of it. He believes that "illegal cell connections" occur where the wolffian duct lies close to the nephro-blastema and the blastema of the pelvic wall. Later the downward growth of the duct carries part of these tissues with it. The frequent location of mixed tumors in kidneys, vagina, and cervix is thus accounted for.

The prognosis of mixed tumors of the cervix is grave. The presence of striped muscle and cartilage must be considered particularly unfavorable (Veit, 106, page 574). Enlargement of the abdomen, cachexia, peritonitis, etc., are encountered, the course resembling that of sarcoma.

V. UTERINE POLYPI

It has been customary to group a number of genetically different conditions under this name. The sole property in common has been the shape, which is bean, tongue or sausage shaped. Included have been localized hyperplasias of the uterine mucosa, pedunculated submucous fibromyomata, conglomerations of nabothian follicles projecting above the surface of the cervix (Schroeder, 177) and even papillomata of the portio vaginalis. In this connection polypi of the mucous membranes are mainly in question.

Corporeal.—In hyperplasia of the endometrium the uterine cavity may be lined with a thick, wavy or even bossed mucosa. Transitions to pedunculated excrescences are common. When multiple, so-called "polypoid endometrium" results (Fig. 185).

Histologically this resembles the rest of the mucosa. Similar projections of mucosa are found in the "dead spaces" between submucous fibroids. Fibrous polypoid growths, containing an increased amount of stroma and with less regular distribution of the mucosal glands, are known as "fibro-adenomatous polypi" (Figs. 186 and 187). They may project as deep red nodules through the external os and be borne into the vagina. They occur most commonly after the menopause. The surface of these growths is usually smooth in contradistinction to those arising in the cervical canal. When exposed to the vaginal secretions the surface epithelium often changes to the squamous type (Fig. 188). If the stroma of the growth contains a preponderance of muscle fibers, the tumors are pedunculated fibromyomata. Cystic changes in the glands are the rule (Figs. 186, 187, 192).

The histology of all these growths resembles that of the uterine mucous membrane closely. The same type of epithelium is found. Both surface and gland epithelium is low cylindrical, with slightly staining cystoplasm

and dark central nucleus. Both epithelium and stroma often show the same cyclical changes as that of the uterine mucosa. In some growths, multi-

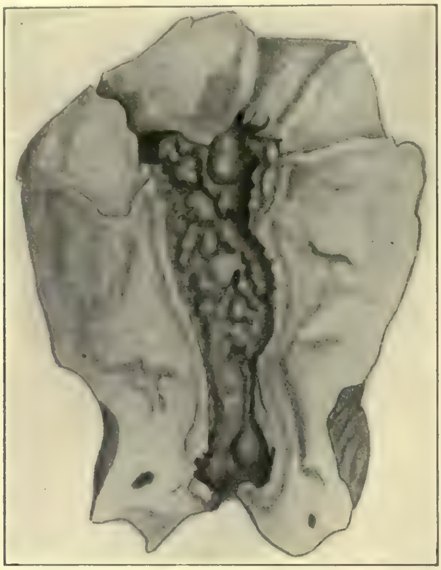

FIG. 185.—POLYPOID ENDOMETRIUM. Uterus removed for menorrhagia. Note diffuse polypoid excrescences.

FIG. 186.—TRANSVERSE SECTION OF THE UTERUS SHOWING MUCOSA (×20.) Cystic endometrium near menopause. Fibro-adenomatous polyp projecting into the lumen of uterus from the left and distending the cavity.

plication of glands produces a picture resembling that of adenoma. In others, the numerous blood vessels give the appearance of erectile tissue. Cavernous polypi or lymphangiectases may predominate.

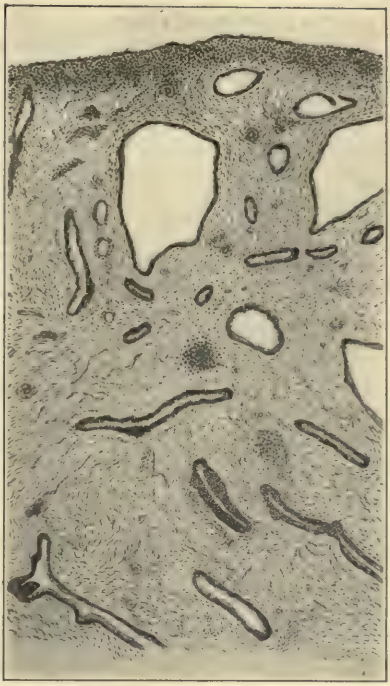

FIG. 187.—FIBRO-ADENOMATOUS POLYP FROM THE CORPUS UTERI. (Medium power.) Note character of mucosa. Cystic degeneration of some glands, apparent multiplicity of layers of epithelium in the glands toward the base of the section (oblique cut).

FIG. 188.—FIBRO-ADENOMATOUS POLYP OF CORPUS UTERI ($\times 10$). Well-marked pedicle to right and below (1) Some glands are cystic, others (2) undilated, show tortuous cork-screw shape. Surface epithelium above (and to left) has become squamous (3).

Cervical.—These polyps more often have a thin pedicle; their surface is commonly less smooth and they are born more early into the vagina than corporeal growths. They may project from the vulva (Fig. 189). Such growths may arise from the portio, in which case glands may be scant and the surface is covered with stratified squamous epithelium. Ordinarily

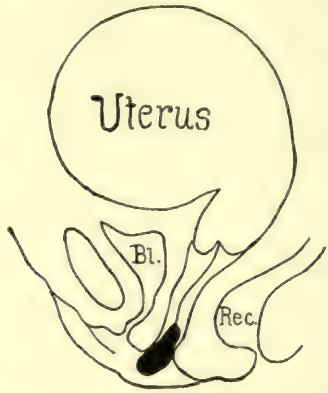

Fig. 189.—Diagrammatic sagittal section of a three months' pregnant uterus. Showing cervical polyp projecting from the vulva attached only by means of a filiform pedicle. The circulation of the polyp was undisturbed.

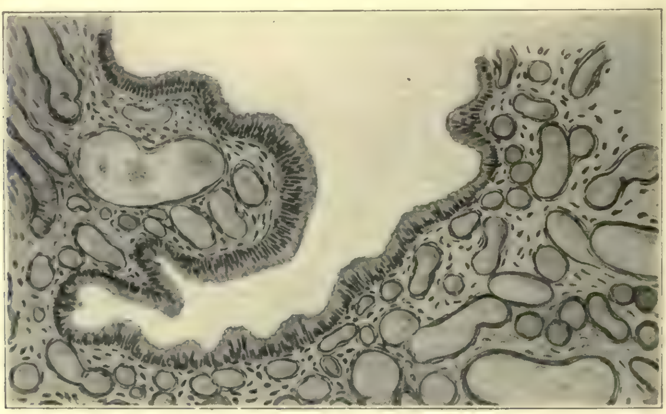

Fig. 190.—Adenomatous cervical polyp with torsion of its pedicle. (Medium power.) Engorgement of the vessels, hemorrhages into the tissue, dilated capillaries almost contiguous are noted. The high columnar cilated epithelium on the surface is characteristically cervical.

both the surface and gland epithelium is that of the cervical canal. The high cylindrical epithelium with clear cytoplasm and dark basal nucleus serves to distinguish the cervical from the corporeal polyp. Secondary changes occur when the polyps project into the vagina.

Secondary Changes.—*Inflammation* evidenced by round-celled and plasma-celled infiltration is common. *Circulatory* disturbances result from

torsion of the pedicle or constriction of it by the cervix. Edema, stasis, hyperemia, extravasation and gangrene result (Fig. 190).

FIG. 191.—ADENOMATOUS CERVICAL POLYP WITH METAPLASIA OF THE EPITHELIUM. 1. Low columnar. 2. Stratified columnar. 3. Transitional and vacuolated squamous.

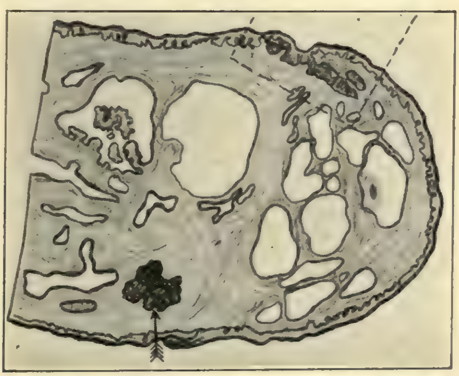

FIG. 192.—FIBROADENOMATOUS CERVICAL POLYP (×15.) The surface is covered with squamous epithelium. The boxed-in area shows epithelial proliferation in direct continuity with the surface. The arrow points to a similar proliferation area in which the continuity with the surface epithelium does not appear. Dilated cervical glands are seen throughout the section.

Cystic changes in the glands are the rule. The lining epithelium may become flattened by pressure. The glands may be closely packed, back to back, so as to produce the picture of an adenomatous growth.

Epithelial Proliferation.—From various causes, among which the irritative probably predominate, bizarre and voluminous proliferation of the surface and gland epithelium may take place. Transitions from low colum-

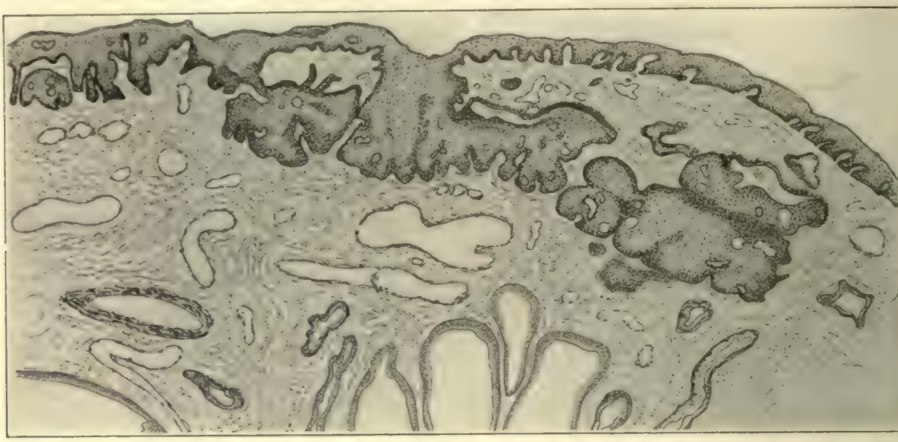

FIG. 193.—FIBRO-ADENOMATOUS CERVICAL POLYP. (High power.) Boxed-in area from Fig. 192. Note epithelial proliferation in direct continuity with the squamous-surface epithelium. Such areas especially when entirely separate as toward the right, are readily confused with a squamous epithelioma. The regular arrangement of the cells toward each other (as in the skin), the absence of polymorphism and of nuclear irregularity differentiate these findings from cancer. Below are dilated cervical glands.

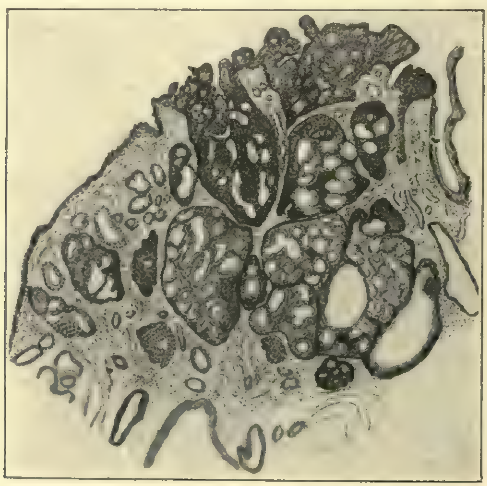

FIG. 194.—CERVICAL POLYP WITH EPITHELIAL PROLIFERATION. (Medium power.) The intermingling of squamous and columnar epithelium together with fenestration, gives a bizarre and malignant appearance to an entirely benign process.

nar, through stratified columnar to squamous epithelium (Fig. 191) are common. Substitution of the columnar by squamous-surface epithelium is the rule when a polyp is born into the vagina (Fig. 193). The squamous epithelium also grows down into the glands partly substituting, partly inter-

mingling or growing beneath the columnar cells (Fig. 194). Pictures such as appear in healing "erosions" of the cervix result (Fig. 144) or quite close imitations of beginning squamous-cell carcinoma are found, especially

FIG. 195.—SARCOMATOUS UTERINE POLYP. (Very low power.) Note area marked for higher power.

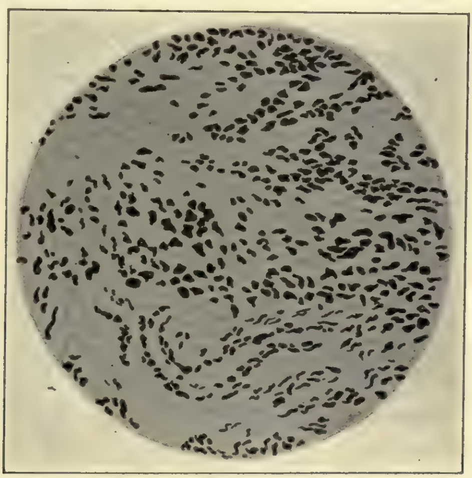

FIG. 196.—SARCOMATOUS UTERINE POLYP. (Medium power.) Higher power from previous section. The nuclei are irregular in size, shape, distribution and tinctorial qualities. This sarcomatous change extends into the pedicle. The section resembles a myosarcoma of the uterine wall.

if, as rarely happens, epithelial pearls occur. The writer has repeatedly seen polypi erroneously diagnosed as cancer because of such changes. The examination of the base of the pedicle may prove decisive.

Malignant changes in polypi are not very frequent. Sarcomatous (p. 247) and carcinomatous (p. 295) changes do, however, occur. The histology is decisive (Figs. 195 and 196).

FIG. 197.—FIBRO-ADENOMATOUS CERVICAL POLYP IN PREGNANCY (×15.) The surface is covered with a high, ciliated columnar epithelium. The glands are typically cervical.

Pregnancy Changes.—During pregnancy the nutrition of polypi is increased. Hence they may grow rapidly. A polyp projecting through the vulva and nourished by a long filiform pedicle is shown in Fig. 189. The stroma (Figs. 197 and 198) and glands of polypi may show marked

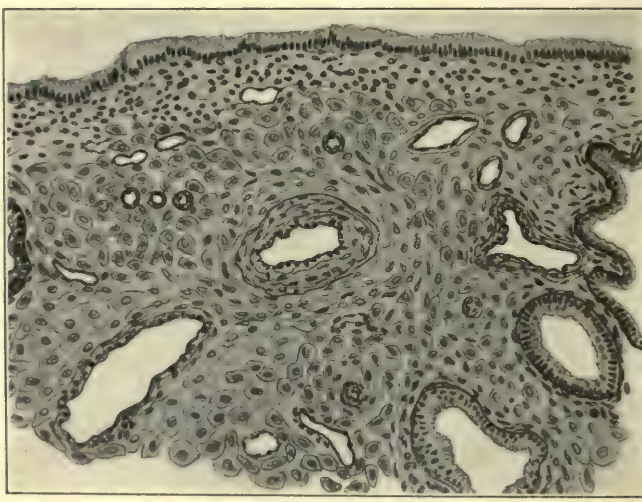

FIG. 198.—FIBRO-ADENOMATOUS CERVICAL POLYP IN PREGNANCY. (High power of Fig. 197.) The stroma of the polyp shows marked decidual changes most evident around the blood vessels. The glands are unchanged. The surface epithelium is typically cervical in character.

decidual reaction irrespective as to whether the type is cervical or corporeal.

Placental polypi will be described under pregnancy. They resemble the above in shape only.

For literature see Hunziker (178), v. Franqué (179), Hitschmann (180).

Polypi cause slight or moderate atypical bleeding and increase of cervical discharge. If large and necrotic, foul discharge may result.

A pure angioma is reported by Boks (180a). It occupied the anterior surface of the uterus and was the size of a child's head.

VI. CARCINOMA OF THE UTERUS

Introductory.—In the female sex efforts to reduce the mortality from cancer of the uterus and breast center mainly in reducing the incidence, by prophylaxis, and in recognizing cases in the early operable stage. Among white females 8.5 per cent of all deaths are due to cancer and of cancerous females 27.6 per cent die of carcinoma of the uterus (McConnel, 181). This means that in the continental United States in 1915, approximately 12,344 women died of cancer of the genital organs (Hoffmann, 182). These truly terrifying numbers emphasize the economic and social importance of the problem. What shall be done to remedy these fatalities? In spite of an intensive campaign in the lay and medical press, Winter, for instance, was able to increase the number of patients who sought competent medical advice by only a small percentage (Döderlein and Krönig, l. c. 37, p. 622).

Precancerous Stage.—The other extreme is represented by the efforts to combat cancer by early recognition of a "precancerous stage." As chronic endocervicitis (Polese, 183), laceration of the cervix, cervical scars, ectropion, eversion with consequent exposure of the delicate lining of the endocervix, scars lacking in vascularity (Theilhaber, 184), as well as corporeal "endometritis," hyperplasia of the endometrium (McCann, 185), and submucous fibroids (McDonald, 186), are commonly found present with or preceding cancer, these conditions are often classed without sharp critique, as precancerous etiological factors.

No statistics taking into consideration the percentage presence of these changes in cancerous and non-cancerous females have ever been compiled. Levine (187) in his analysis of 613 cases of cancer of the uterus, found two cases of cervical cancer in which the cervix had been repaired. Radical pathologists (Schauenstein, 188; Schottländer, l. c. 116, p. 527, Ewing, 189, Rubin, 190) classify as beginning cancer conditions which, lacking as we do absolute histological criteria of early malignancy, may as well prove to be harmless epithelial proliferations.

I have repeatedly diagnosticated such conditions in opposition to other opinions, as non-malignant or merely suspicious, and the clinical course has sustained the contention. For example, a fat woman of thirty-two, who was a poor operative risk, consulted me. She was suffering from a severely eroded cervix. She brought along the slide containing a section of the cervix (Fig. 210) which had been excised and diagnosed as cancer by three

pathologists, one of international repute. Her room had been engaged at the hospital and a gynecologist of little experience was prepared to perform the radical operation. The specimen showed a slanting section of an inflamed portio mucosa. In the course of three weeks three further excisions of specimens were made by the writer, all showing non-malignant erosions (Fig. 142, p. 199). During five years of observation no carcinoma has developed.

The mere fact that gynecologists so rarely see cases of early cancer of the cervix (see rarity in large statistics of Cullen, l. c. 66; Schottländer and Kermauner, l. c., 190a; Frankl, l. c. 22, p. 81, saw only 34 early cases in 1007 specimens), proves that the onset is insidious. In a clinical experience of twenty years, the writer has seen but two cases of early cancer of the cervix in which histological examination was really needed to confirm the diagnosis. In all cancer cases the clinical criteria were unmistakable. In all the numerous cases in which doubtful cervical conditions were encountered, examination of excised portions showed non-malignant conditions.

Schottländer (191) reports 2 per cent accidental finds of cancer in the routine examination of uterine specimens. The criteria of "beginning cancer" employed by this author appear doubtful to the writer.

For this reason the tendency to remove uteri on suspicion only—based upon the as yet unproven theory that excision of cervical specimens and exploratory curettage of the cervix and fundus uteri are prone to disseminate cancerous infection (for opposite view see Wood (192), also for case where curettage failed to disclose the cancer see Gónin, 192a), is to be strongly condemned. It has led to a craze for hysterectomy comparable to the "Battey craze for oöphorectomy" of the late "70's." "Occasional gynecologists" whose experience and clinical judgment are particularly insufficient, have utilized the support offered by "precancerous" dangers and the bogie of dissemination by exploratory curettage to persuade the laity to submit to unnecessary radicalism. The question arises whether the mortality of complete hysterectomy (3 to 5 per cent, Miller (193), in skilled hands) does not far exceeed the problematic prophylactic gain.

Efforts should be made to have women submit to biyearly examination. If the profession is then taught to recognize cancer when still in an operable stage, improved results may be looked for. Repeatedly it happens that the family physician fails to make a vaginal examination, or not recognizing the condition, continues "local treatments" until the cancer is inoperable. Many women, fearing to be told that they have cancer, disregard hemorrhage and foul discharge until intolerable pain forces them to seek belated advice.

Irregular bleeding, especially after onset of menopause or after trauma, post coitus, etc., and beef-watery discharge require immediate vaginal examination (digital and specular) by a competent physician.

Of the so-called "precancerous" conditions which require microscopical

examination, *persistent erosions* (see page 198) are of greatest importance. Friedländer (194) in 1877 pointed out the frequency of so-called "benign epithelial proliferations." In the cervix, healing erosions which show intermingling of squamous and cylindrical epithelium, glands filled with squamous-cell plugs, and surrounding areas of inflammation, prove stumbling blocks to the inexperienced. Good and numerous sections will show absence of downgrowth of the epithelium and infrequent mitoses. Cuts slanting to the surface (Fig. 210) will give most bewildering pictures.

A carcinoma is unmistakable, and in accord with Lubarsch (195), *the writer must insist that, while a specimen may be suspicious, in a given case we are dealing either with a cancer or not.* Ewing's contention that we may be dealing with a condition "in the process of becoming cancer" (196) may be theoretically true, but cannot at present be proved. It has been too often used as a basis for unnecessary radical removal. There is no reason why such a case cannot be watched by a competent observer for a few weeks, when a new exploratory excision can be made, or until more definite—though still early—signs develop. In principle at least (though few patients or physicians would show the necessary patience) it is preferable to curet 20 times in 10 years before finding malignant changes as Baecker (197) did, rather than to fill the laboratory shelves with histologically normal uteri, as is the present tendency. Stone (198) gives an excellent review of the more radical opinions on precancerous lesions, although his interpretations of his own cases are conservative.

A short and masterly review of the criteria between "epithelial changes and beginning cancer in the female genital apparatus" has recently been given by the father of modern Gynecological Pathology, Ruge senior (199). He has the true critical insight based upon experience and knowledge of normal conditions, congenital variations and pathological changes not yet characteristic of malignancy.

The criteria given by Schauenstein, Schottländer, Ewing and Rubin (*vide ante*) for the recognition of incipient carcinoma are in substance as follows:

1. Irregular arrangement of cells.
2. Loss of cell boundary.
3. Abnormally close juxtaposition of cells.
4. Changes in chromatin network.
5. Change in protoplasm toward stains (eosinophilia).

No attempt can be made in these pages to give even an outline of the enormous amount of work performed to clarify the cancer problem. Only facts essential to the discussion will be considered.

Classifications of Carcinoma.—Classifications according to morphology, histogenesis and biology are numerous and unsatisfactory. The reader is referred to books on general pathology, to special treatises dealing with neoplasms such as Borst (200), Ewing (l. c. 98), or to the monographs of Cullen (l. c. 66) and Schottländer and Kermauner (l. c. 190a), etc.

The classification employed by the author is based purely upon morphology in order to describe conditions. Occasionally, for convenience, such obsolete but well substantiated terms as "medullary," "scirrhus" or "plexiform" are employed.

Although clinical differences exist between cancer of the cervix and cancer of the body of the uterus, all varieties to be described occur indifferently, though with greatly varying frequence, in these different locations. Likewise the clinical malignancy varies according to locality and not according to morphology (vide adenocarcinoma of cervix and body).

The cancers to be discussed show the characteristics of two cell types, that of the surface epithelium of the skin and mucous membranes, *epithelioma* (or epidermoid cancer) and that of the *cylindrical* and *gland cell* type of carcinoma ("adenoma malignum," adenocarcinoma, and carcinoma simplex).

Epithelioma occurs especially on the portio vaginalis and within the cervical canal. The *squamous epithelioma* is composed of flattened epithelium. This shows cornification, pearl formation, prickle cells and intercellular fibrils when most typical (Fig. 205), but may appear in the guise of large polyhedral cells in alveolar distribution in less typical cases (Fig. 206), often showing a marked polymorphism with tendency to giant-cell formation (Fig. 208). Different parts of the same growth may show different characteristics.

The less well differentiated forms are uncommon. In these tumors the cells are smaller, more polyhedral or spindle forms, closely packed and devoid of prickle cells (Krompecher's basal cell cancer, 201, 201a).

Epithelioma shows *macroscopically* as an indurated nodule, an excavated ulcer or a cauliflower growth. *Microscopically,* plexiform, papillary, pseudoglandular or alveolar shape is assumed without in any way affecting the clinical dignity of the growth.

Cylindrical-cell carcinoma may, when highly differentiated, follow in type the high, clear cylindrical cell with basal nucleus characteristic of the cervical canal—seen in *"adenoma"* and *"adenoma malignum" of the cervix* (Figs. 213 and 216), or the shorter, more deeply staining cell with central nucleus as found in the corpus—*"adenoma malignum"* corporis (Fig. 229), but eventually by anaplastic changes (undifferentiation) becomes *adenocarcinoma* (Fig. 231), or even *solid carcinoma* (C. simplex, C. medullare) (Fig. 232). Usually fluid transitions from one type to another are not difficult to demonstrate, occasionally purely adenomatous forms have been found in the cervix. Clinically, these adenomas also are malignant.

Combinations of all types and *transitions* are not uncommon. Thus cornification and epithelial pearls may be found in areas of adenocarcinoma of the cervix or corpus uteri (Figs. 211 and 233). These are explained by *metaplasia* of cylindrical cells into squamous ones.

Schottländer and Kermauner (l. c. 190a, p. 478) despairing of correct

classification, have rubricated cancer as *primarily solid* and *primarily glandular*. Under solid cancer they distinguish ripe, middle ripe and unripe forms according to the presence of prickle cells, cornification and small, irregular cell types respectively. Under primarily glandular, they give as subdivision, secondarily solid types which embrace the transitions referred to above under combination forms.

According to direction of growth these authors speak of *exophytic* forms which protrude as papillary tumors, while infiltrating growths are spoken of as *endophytic*. Sampson (202) uses the terms *everting* and *inverting* to convey the same description, although these terms are more often employed to describe the microscopic development of glands as seen in the normal endometrium and in adenocarcinoma (Winter, 203).

Fuller details concerning the current classifications can be found in Kaufmann (l. c. 125a), Aschoff (204), Adami (205), etc.

Although cervical and corporeal cancers occur in the same organ, their course, method of extension, duration, malignancy, etc., differ so widely that they must be discussed separately.

CANCER OF THE CERVIX OF THE UTERUS

Attempts to divide cervical cancers into those originating in the portio vaginalis and those of endocervical origin as first proposed by Ruge and Veit, are uncertain and unprofitable (Krukenberg, 205a). All cervical cancers will be discussed together because as the region of the external os is regularly involved, it is impossible to differentiate endocervical from portio cancers.

The age distribution of cervical carcinoma is well illustrated by Peterson's statistics (206) in 406 cases of squamous cell and 94 adenocarcinomas, and of Koblanck's (207) statistics of 6071 cases collected from the literature.

PETERSON

Ages	Number of Cases	Percentage	
20–25	6	1.4	
25–30	15	3.6	
30–35	31	7.6	..21.3%
35–40	56	13.7	
40–45	79	19.4	..32.4%
45–50	53	13.0	
50–55	65	16.0	...28.8%
55–60	52	12.8	
60–65	29	7.1	
65–70	16	3.4	
70–75	1	.2	
75–80	2	.4	
80–85	1	.2	

KOBLANCK

Ages	Number of Cases	Percentage
10–19	2	
20–29	220	
30–39	1472	24
40–49	2168	33.7
50–59	1464	24
60–69	531	
70–79	214	

The average age in Peterson's series is 45.5 years. The average age of 94 cases of adenocarcinoma of the fundus in this same series of 500 cases was 54.1 years. Peterson finds the maximum incidence at the age period of 40–45 years, Koblanck 40–49 and Levine (l. c. 187) between 45 and 60 years. As will be seen later, fundal carcinoma is commonest 10 to 15 years later, 50–59 years.

The youngest patient with carcinoma of the cervix that is fully substantiated is that of Glöckner (208) in a girl of 8 years. Here adenocarcinoma was diagnosed by R. Meyer and by Ruge. Findley (209) mentions a case at 6 months and Adams (210) at 2½ years. The latter case was classified as a mixed tumor by the Pathological Committee of the Royal Academy of Medicine and can therefore be excluded, while Findley's case was seen at Bumm's clinic (personal communication) and was substantiated by R. Meyer, Aschheim Bumm (211).

The influence of preceding pregnancies has been much emphasized in connection with carcinoma of the cervix, while in corpus carcinoma a higher proportion of nulliparae are found (Falk, 211a).

Deelman (212), in contradistinction to the older writers, appears to be correct in his contention that the number of children does not seem to have any influence on the incidence of cancer of the cervix; but the fact that there has been at least one childbirth does have a big influence. In other words, *one childbirth is as effective a cause as repeated labors.* The older authors worked out the number of childbirths to a given patient; Gusserow, 4.5 labors; Hofmeier, 5.02 confinements to each carcinoma of cervix (213); Theilhaber and Edelberg (214) say that women with one labor are seen in 8 per cent, with 6 labors in 13 per cent, and nulliparae in 2.9 per cent. Levine (l. c. 187) has shown that the ratio of married women to single women at 45 years of age is 7 to 1 while that of cancerous multiparae to nulliparae is as 7.5 to 1—no appreciable difference. Hoffman (l. c., 182, p. 99) asserts that the married suffered 73 per cent more from cancer of the uterus than the unmarried.

The frequency of occurrence of uterine carcinoma according to Camperman (215) is 4 per cent of all gynecological cases. To show the proportion to other cancer deaths in women, McConnel's (l. c. 181) table is appended.

Among women the cancer deaths in 1000 cases are distributed as follows:

276.2	Uterus
244.7	Stomach
157.8	Breast
125.9	Liver
76.9	Abdomen
35.5	Rectum

Of genital cancers over 93 per cent were uterine (Hecht, 216) as found in Vienna Hospitals. This seems an unduly high proportion. Of uterine cancers, cervical occur in from 81.2 per cent (Peterson, l. c. 206) to 90 per cent (Koblanck, l. c. 207, p. 672).

Precancerous conditions have been discussed on page 271. The favorite site is in the region of the external os. The exact point of origin is obliterated early. Erosions, lacerations and eversions are generally blamed. Whether they are causal or merely coincidental does not appear determined.

Macroscopic Appearance of Cancer of the Cervix.—*The earliest stage,* but rarely seen, is a *hard induration* of the cervix without loss of tissue. A hard nodule may be felt under the intact epithelium, the so-called central nodule of Ruge and Veit (occurring only in 0.4 per cent, Bennecke (217) in material of 1249 cases), or if the exophytic type is present, small branching papillae (1 to 2 mm. in height) may be noted.

From such a small beginning the well-known *cauliflower growths* originate. They may occupy both cervical lips and involve the vagina, forming huge friable red to pink, grapelike masses which bleed upon the slightest touch. The cervical tissue is also involved, appearing translucent grayish-white on section. Comedolike cell nests, or "cancer juice," if the nests are smaller, can be expressed from the surface of the cut (medullary type), the scirrhous forms being harder and less juicy.

More commonly the patient is first seen when disintegration of the cervix due to breaking down of the growth has begun. Part or all of the infravaginal portion of the cervix may have disappeared. A hard, irregular, nodular cavity formed above by some part of the cervix, and laterally by the infiltrated vaginal vaults, soon develops. The growth bleeds readily to the touch. The broad ligament may show induration. The limits of extension along the vagina are elevated, nodular and hard. The upper limits of the intracervical parts of the tumor cannot be determined until the specimen is cut open. Usually the process appears to halt at the internal os but Schottländer and Kermauner (l. c. 190a, p. 448), on microscopic examination, found the corpus involved in nearly 50 per cent of cases.

The gross appearance is most varied, depending upon the relative amount of induration and excavation, the presence or absence of cauliflower projections and upon the direction of extension. In some cases the portio may

appear almost intact (Fig. 200) on section showing complete involvement of the circumference of the cervical canal (Fig. 199b). Again a large cauliflower mass may have only a small pedicle attached to the cervix (Fig. 202). In the harder, more fibrous forms, retraction of the tissues may hide the loss of substance, by puckering and shrinking of the vagina, as in senile vaginitis.

The far advanced cases present a foul-smelling, indurated crater whose walls are formed by cancerous tissue which may extend laterally to the pelvic wall. Eventually indescribable cloacae which drain uterus, bladder or ureters and rectum may develop, especially if radium treatment is employed after the vesicovaginal and rectovaginal septa are already infiltrated by cancer. Cullen (l. c. 66) mentions suppurating deep lymphatic glands draining into the cloaca. Küstner (218) describes prolapse of the small intestine through the eroded posterior cul-de-sac.

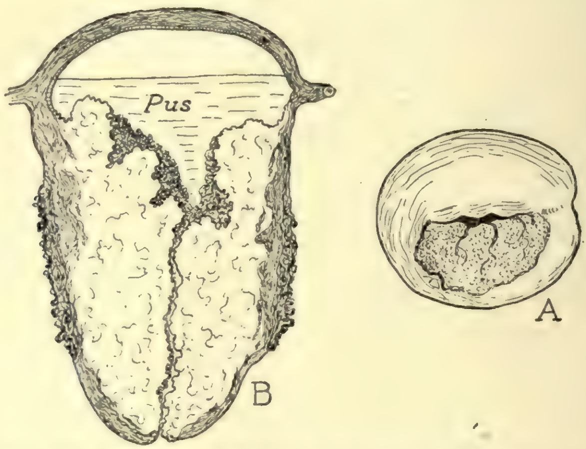

FIG. 199.—A. VIEW OF THE PORTIO FROM BELOW SHOWING INVOLVEMENT OF THE POSTERIOR LIP, APPARENTLY VERY LIMITED IN EXTENT. (×½.) Low papillae, indurated, bleeding readily to touch. B. TRANSVERSE LONGITUDINAL SECTION OF THE SAME UTERUS. (×⅓.) Showing almost entire substitution of uterine wall by the cancer with functional occlusion of canal and pyometra.

The duration of untreated cancer of the cervix is rather short. According to Wilson (l. c. 241, II, p. 551), it averages one year and eight months. On the other hand, cases have been observed for seven (Wells, 219) to fifteen years (Camperman, l. c. 215). Death may supervene from cachexia, due to absorption from the toxic and infected local growth, to hemorrhage, peritonitis, pyelonephritis due to obstruction, chronic uremia or some intercurrent terminal disease such as pneumonia.

Regression.—Cases authenticated by microscopical examination have apparently recovered after no interference or after incomplete or palliative operations (Lömer, Weindeler, Brettauer, Rhodenburg, 220). Such instances are most uncommon and do not vitiate the general conclusion that cancer, to be cured, must be completely removed.

Extension of Cervical Cancer in Operable Cases.—The involvement of the *corpus* in nearly 50 per cent of cases has been mentioned.

VAGINA.—The same authors (l. c. 190a, p. 596) found the vagina involved in 36 per cent of solid cancers and in 28 per cent of adenocarcinoma; Brunet (*221*) in 43 per cent. Usually the growth was parenchymatous (i.e., subepithelial), more rarely a surface extension was noted.

FIG. 200.

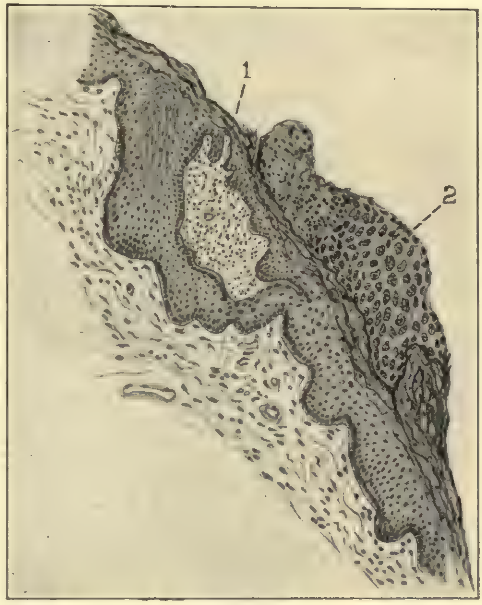

FIG. 201.

FIG. 200.—ADVANCED CARCINOMA OF THE CERVICAL CANAL WITH INTACT PORTIO. (×10.) The carcinoma has left a mere shell of the cervix although the entire cervical canal is deeply eroded. On the portio is a small surface implant. 1. Carcinoma lining cervical canal. 2. Implant on portio.

FIG. 201.—High Power from Fig. 200.—SURFACE IMPLANTATION ON THE PORTIO VAGINALIS. Where the superficial surface epithelium is abraded, a nest of cancer cells has become adherent and judging by the appearance of the cells, is continuing to grow. The connective tissue surrounded by normal squamous epithelium is an artefact, produced by the core of a papilla being cut obliquely by the plane of the section. 1. Pointing toward connective tissue core. 2. Surface implant of cancer.

PARAMETRIUM.—This includes the pericervical connective tissue and the bases of the broad ligaments as well as the paravaginal tissues and was found involved in 94 and cancer-free in 43 (31 per cent). Kundrat (*222*) found 55 per cent involvement.

The extension most commonly occurs by continuity of growth, more rarely metastatically or by a combination of both (Kundrat, l. c., *222*). The tumor may advance in the tissue spaces, lymph channels (Fig. 203), along nerves (Brunet, l. c. *221*), or blood vessel (veins—six times in 55 cases, Scheib, *223*), or more rarely arteries (Goldmann, *223*a).

The parametria are almost regularly infected with *bacteria* in ulcerating cases of cancer and not infrequently in non-ulcerating cases (Heimann 224). This accounts for the foudroyant streptococcus peritonitis not infrequently encountered post operatively (39 cases in 500 of Wertheim's series, 225, p. 187). The regional lymph glands not infrequently harbor streptococci or other bacteria.

Fig. 202.—Section of exophytic adenocarcinoma of cervix. (×20.) (Photomicrograph.) Showing large cauliflower growth with pedunculated attachment to the portio. Note cancer alveoli in the center of the cervical tissue.

The small discrete (encapsulated) and diffuse collections of *lymphoid tissue* found scattered in the parametria are very rarely cancerous (Sampson, l. c. 202). Often such foci are mistaken for a leucocytic infiltration (Schottländer and Kermauner, l. c. 190a, p. 602). The lymph nodes may be intravascular (i.e., projecting into the lymph vessels).

Lymph Glands.—The statistics vary considerably. Kundrat (l. c. 222) found 32.5 per cent of 80 cases with lymph glands involved, Sampson

(226) 47 per cent in 19 cases, Wertheim (l. c. 225, p. 197) 25 per cent in 500 cases (removed at operation), Schottländer and Kermauner (l. c. 190a, p. 457) 43.8 per çent in 73 cases. If the percentage is derived from grossly enlarged glands removed at operation and examined microscopically 25 to

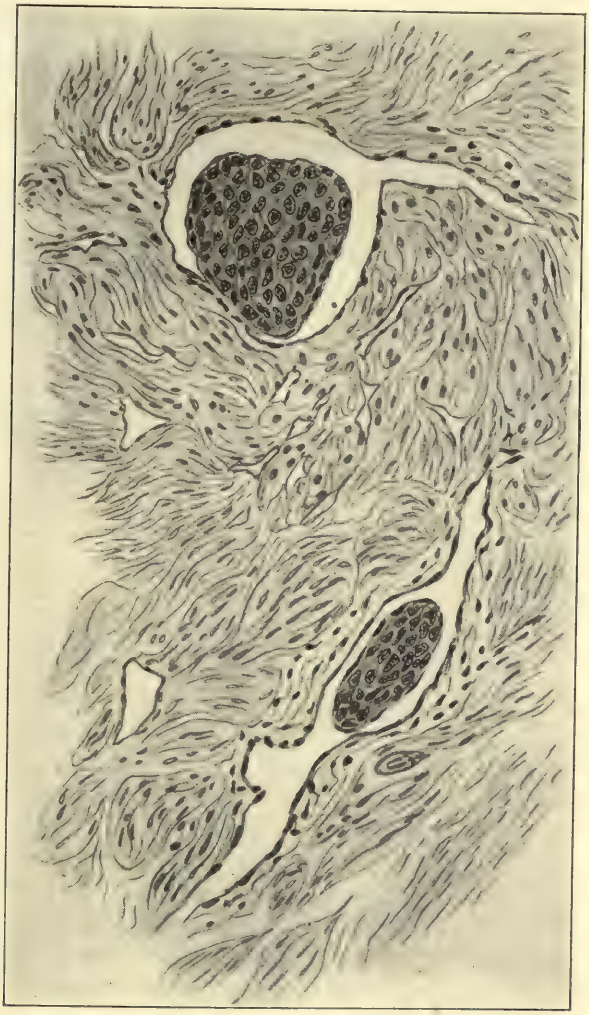

FIG. 203.—CARCINOMA OF THE UTERUS. EXTENSION OF CANCER CELLS WITHIN LYMPH SPACES. (High power.) Above, the section passes transversly through an endothelially lined space, below longitudinally. In each of these lymph vessels is a mass of cancer cells.

27 per cent are found involved; serial section of parametria and all glands appears to give the higher percentages of 43 to 47 per cent or more.

Winter (227) in 44 autopsies of cases which died immediately after operation, where the cancer was still limited to the uterus, found only 2 cases of gland involvement. Where the tumor had not penetrated the para-

metrium, lymph gland involvement was found in from 5 to 19 per cent, if the parametrium was involved the percentage rose to 35 to 50 per cent (Döderlein and Krönig, l. c. 37, p. 611). In more advanced cases lumbar and aortic, retroperitoneal, thoracic and even supraclavicular glands may be affected (Kaufmann, l. c. 125a, II, p. 1029). In 35 cases examined at a complete post mortem immediately after death following operation 37 per cent showed cancerous lymph glands (Döderlein and Krönig, l. c. 37, p. 611).

Ureteral glands in the parametrium, where the ureter is crossed by the uterine arteries, must always be looked for. They were found 8 times in 41 cases and 3 times were cancerous (Sampson, l. c., 226). Brunet (l. c. 221) found this gland present in 60 per cent.

For literature on lymph glands see Gellhorn (227) and Cigheri (227a).

Enlargement of lymph glands does not signify cancerous involvement. Irritation from the cancer toxins, or from breaking down and infected growths (bacteria) produces gland enlargement. Wertheim (l. c. 225, p. 163) declares that the long spindle-shaped lymphatic glands found along lymph vessels, are never cancerous, but glands of even the size of a pea may already be infected. Coincidental tuberculosis has been occasionally reported.

Glandular structures within lymph glands consisting of tubules lined by cuboidal or cylindrical ciliated epithelium were reported by Ries (228), and interpreted by him as remains of wolffian structures, also by Albrecht and Arzt (229). As Kaufmann (l. c. 125a, p. 1030) reports finding the same structures in lymph glands of the axilla and neck, a wolffian derivation may be definitely excluded. They are found in non-cancer cases (Falkner 230). R. Meyer (231) considers them due to inflammatory reaction of the lymph endothelium (Sitzenfrey, 232). The mistaking of these structures for metastases of adenocarcinoma is unlikely if their possible presence is remembered, as the lining cells are more uniform in shape and size and resemble endothelioma more than carcinoma.

Metastases of cancer in lymph nodes begin near the convex periphery (Kroemer, 233) (Fig. 204).

Irregular mitoses, a tendency to giant cell formation and less connective tissue than in the primary tumor are often noted (Brunet, l. c. 221).

Adjacent Organs.—If much involvement has occurred the cases are no longer operable.

Schottländer and Kermauner (l. c. 190a, p. 609) find evidence of the involvement of the *bladder musculature* only 4 times. Brunet (l .c. 221), on the other hand, in 22 cases of bladder injury (of 70 radical operations), found cancer in the anterior parametrium 10 times, and three times invading the muscular bladder wall. Evidently much depends upon the indications for operability.

The ureter was affected in only 2 cases of Schottländer and Kermauner and in the literature they found only 6 others mentioned (l. c. 190a, p. 610,

Offergeld, 234). This organ, though repeatedly found embedded in cancerous masses, appears to possess unusual resistance.

The *rectum* can be involved, extension by means of the connective tissue to Douglas's cul-de-sac and thence to the *general peritoneal* cavity can occur (Kotzareff, 234a).

A few cases of *surface extension* over the entire genital tract (vagina, tubes, ovaries) are reported (Gellhorn, 235).

The *fallopian tubes* are rarely involved. Cullen had one case (l. c. 66, p. 157), Schottländer and Kermauner, two (l. c. 190a, p. 618), Kundrat (l. c. 222) two cases.

FIG. 204.—LYMPH GLAND METASTASES FROM CARCINOMA OF THE CERVIX. 1. Lymphoid tissue. 2. Cancer cells near periphery of the gland. 3. Connective tissue surrounding the gland. 4. Periglandular fat.

The *ovaries* in Cullen's series of operable cases were never involved (l. c. 66, p. 155), in Schottländer and Kermauner's (l. c. 190a, p. 460) only twice.

OPERABILITY, OPERATIVE OBSERVATIONS AND RESULTS.—Wertheim (l. c. 225), in his series of 500 abdominal operative cases, found about half of the cases operable (48.9 per cent). In 16 per cent exploration was required to determine operability (not operable if parametria show wide infiltration, if extra pelvic glands are involved, etc.) as inflammatory infiltration often makes the parametria appear cancerous.

There were no more recurrences in the youthful than in the aged, no more in the pregnant than in the non-pregnant. Squamous-cell cancer showed no greater malignancy than adenocarcinoma. Of 142 cases with lymph glands free, 100 remained well (recurrence 29.5 per cent); of 41

with lymph glands removed at operation, but found cancerous, only 5 remained well (recurrence in 87.8 per cent). Absolute cure (according to Winter's (236) formula) was 18.4 per cent.

Schauta (237) was able to operate 51.3 per cent by the extended vaginal route. His absolute cures were 16.9 per cent (445 operations), and in 1917 had risen to 21.9 per cent.

Recurrences arise locally, frequently from incomplete operations along the vaginal cuff and in the parametrium, close to the pelvic wall. Regional or extra pelvic lymph glands may be affected.

So-called *implantation metastases* in the scars of a Schuchard incision (Stickel, 238), or in the scars of the abdominal wound (Flaischeln, 239) were more frequent before the routine cauterization of the tumor was practiced at operation. Franz (240) mentions a cure of five years' duration after seven successive operations for recurrence. Most operators no longer reoperate for pelvic recurrences. Zweifel (240a), reviewing Franz's operations for recurrences, found 5 of 17 patients surviving on an average of seven and one-half years.

Wertheim (l. c., 225, p. 191), in 78 recurrences, as is the common observation, found the time elapsed was as follows:

WERTHEIM

1 year	41
2 years	24
3 years	6
4 years	4
5 years	3

Weibel (240b), reviewing all of Wertheim's cases, found the following:

WEIBEL

1 year	50% of all recurrences
2 years	25
3 years	11.5
4 years	3.4
5 years	3.4
6 years	2.8
7 years	3.4

After the eighth year he never saw recurrences.

Pyometra occurs not infrequently when the drainage of the uterus is interfered with or infection supervenes together with muscular atrophy (Fig. 199) (Wilson, 241). Rupture of the pus into the abdominal cavity has been reported by Oberndorfer (242). Physometra (Strassman,

243), hematometra (Ottaw, 244), mucometra (Birnbaum, 245), and hydrometra (Graves, 246) are recorded.

The association of cancer of the cervix with myoma appears accidental. See fibromyoma, page 243.

Stump Cancers.—Occurrence of cervical cancer in the stump left after supravaginal hysterectomy was reported by Winter (248), Chaput (249), etc. Polak (250) gathered 256 cases from America recently. He advises the complete operation in all myomectomies. Fehim (247) reports intracervical cancers occurring in the stump as late as five to fifteen years after supravaginal hysterectomy.

Cancer and Pregnancy.—On account of the advanced age of most patients suffering from cervical cancer pregnancy is not very frequent (1 in 2000 pregnancies, Sarwey (250a); 1 in 1762, Williams (250b), who found pregnancy once in every 63.5 cases of cancer).

Of 603 cases he collected, 261 died in or after labor. In the older literature patients died undelivered or from uterine rupture (Herman, 251). See Sarwey (l. c. 250a), 180 cases, of whom 13 died undelivered and 11 of ruptura uteri, 58 children alive. In modern days the results of operation are almost as good as in the non-pregnant (Hense (252), or as good, Wertheim (l. c. (225), 8 cases in 500 operations).

Extra-uterine pregnancy may occur (see literature in Wilson, 253) but is very rare.

Cancer in prolapse, see page 174.

Cancer a deux appears apocryphal. Williams (254) in 134 men with cancer of the penis, found only one wife with uterine cancer, and no husband of 180 women with uterine cancer had penile carcinoma. Wolowski (255) reports such a couple.

So-called *contact cancers* ("abklatsch") are likewise doubtful. Hartmann and Lecène (256), Hellendal (257) mention an adenocarcinoma of the cervix with metastasis in the vagina. Usually subepithelial lymphatic connection or true metastases account for the condition.

Cancer can occur in *malformed uteri* (Melson, 258), Rossa (259) cancer in bicornate uterus with pyometra, Buist and Valentine (260) four cases in double uteri. Orthman (261), Pick 262). For literature see v. Rosthorn (263).

Multiple cancers have been repeatedly observed. Great caution must be observed in judging of the authenticity of these cases. Kaufmann (l. c., 136, p. 1031) reports cancer of the stomach and portio vaginalis; of gall bladder and portio (Tsuji, 264). Where cancer of cervix and corpus are reported coincidentally great doubt must always be entertained (Warstat (265) Case II; Hofbauer, 266).

Tuberculosis and cancer are not infrequently associated, more often with corporeal carcinoma, however. Hoehne and also Croner (267) reported corporeal tuberculosis and carcinoma portionis, Wallert (267a) cervix cancer and cervix tuberculosis.

Extension of Cancer of the Cervix; Autopsy Material.—These reports show the final termination of cancer of the uterus. Toward the end uterine cancer metastasizes in 25 per cent of cases (Willimsky (268) 1122 cases). Leitch (269) in 915 autopsies, found no metastases (including glandular ones) outside the pelvis, in 55 per cent.

In 255 cases, Winter (270) found metastases in the

Liver, 24	9 per cent
Lung, 18	7 per cent
Kidney, 9	3.5 per cent
Stomach, 4	1.5 per cent
Intestine, 4	1.5 per cent
Thyroid, 5	1.9 per cent

Albers-Schoenberg (271) in 564 autopsies found the liver affected in 13.8 per cent; the heart, in 0.7 per cent. Terminally the ovaries (in 3 inoperable cases, Cullen, l. c., 66, p. 155) are more often involved; Blau (272) 25 times in 93 autopsies.

Metastases in rare situations, are spine (Kamann, 273), brain, muscle, skin (Offergeld, 274), ureter, supraclavicular glands, ductus thoracicus (Offergeld, l. c., 234), kneejoint (Schiller, 275). Williams (l. c. 254) in 78 autopsies found extension to bladder in 56, vesicovaginal fistula in 29, extension to rectum in 19, rectovaginal fistulae 10, hydronephroses 67.

Blau (l. c. 272) in 87 autopsies, found the peritoneum involved in 16 (9 times limited to Douglas's cul-de-sac, 7 times involving the entire peritoneal cavity).

Carcinoma of Gärtner's duct is recorded by R. Meyer (276), arising from bilateral ducts in their cervical portion, forming a tumor in the anterior cervical wall with metastases in the vagina. The type varied from adenoma, through papillomatous portions, to true adenocarcinoma.

Histology.—*Squamous cell cancer* is the commonest variety in the cervix.

Schottländer and Kermauner (l. c. 190a, p. 498) in 140 cases, 83 per cent; Cullen in 176 cases, 70 per cent; Obata, (277) of 134 primarily solid cancers, 120 were of the collum, and only 11 corporeal; Wilson (l. c. 241, p. 445) of 136 cases, 92 per cent squamous.

It may appear as a typical ripe epithelioma with prickle cells, cornification and pearls (Fig. 205). It may occur in the guise of alveolar cancer (Fig. 206) or in an endotheliomatous distribution along the lymph and tissue spaces (Fig. 213), with little or no cornification and with neither evidence of prickle cells nor of the three layers characteristic of the epithelium of the skin. Such forms are called unripe forms.

FIG. 205.—CARCINOMA OF THE CERVIX. FULLY RIPE TYPE. (High power.) Showing pearls, cornification and alveoli closely imitating the normal distribution of squamous epithelium.

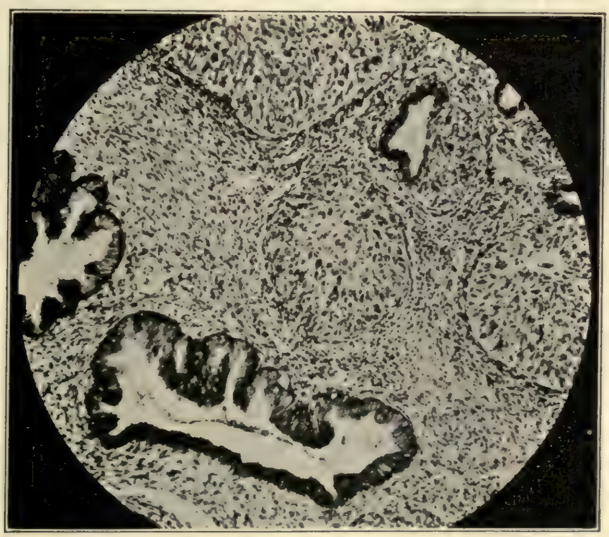

FIG. 206.—SQUAMOUS-CELL CARCINOMA OF THE CERVIX. (Photomicrograph H. P.) Above three alveoli shown in close proximity to normal cervical glands (below).

Great variations are seen in the size of the alveoli and of their component cells. This, together with differences in the amount of connective tissue present, gives origin to a large number of small and large alveolar, diffuse and scirrhous types. The less connective tissue is present, the more medullary the cancer, and the more difficult to distinguish from sarcoma. This difficulty is increased by the polymorphism of the cells. See Fig. 208, in which pyknosis, hyperchromatism and giant-cell formation are unusually developed. Syncytial complexes, indistinguishable from chorionepithelioma, may be found (Frank, 278).

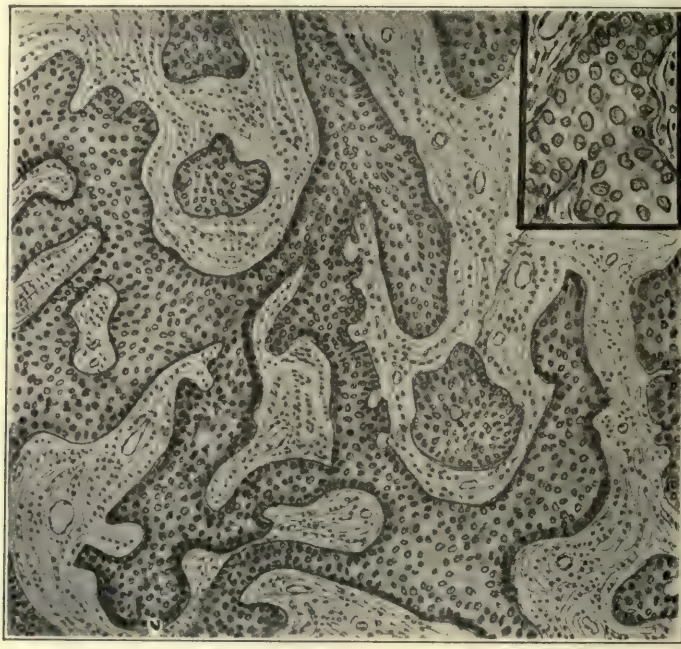

FIG. 207.—SOLID SQUAMOUS CELL CARCINOMA OF THE CERVIX. (Medium and high power.) Showing lymphatic distribution. This was a papillary tumor which in spots, not shown in figure, had medullary areas with cornifications.

Oblique sections or section "on the flat" will give peculiar and confusing pictures (Fig. 209). Normal cervical epithelium cut at the junction with the corium also gives cancerlike pictures (Fig. 210).

Epithelioma showing transitions to adenomatous types (or the converse) is not uncommon. The cells may be squamous with glandlike distribution and show evidence of cornification (Fig. 211).

Cylindrical cell carcinoma, like epithelioma, is found in ripe and unripe forms.

It occurs less frequently than squamous carcinoma (Schottländer and Kermauner, l. c. 190a, p. 479), in 140 cases only 17 per cent. Obata (l. c. 277) of 112 primarily

glandular cancers, found 88 corpus, 16 cervix, 1 portio, and 7 unclassifiable. Cullen (l. c. 66, p. 646) of 53, found 35 of the body.

So-called "*adenoma malignum*" is the ripest. A small number of cases with tortuous glands lined by a single layer of epithelium are on record as *adenoma*, Gebhard (l. c. 31, p. 145), Cullen (l. c. 66), Obata (l. c. 277), Limnell (279), 13 cases. (Figs. 212 and 213.)

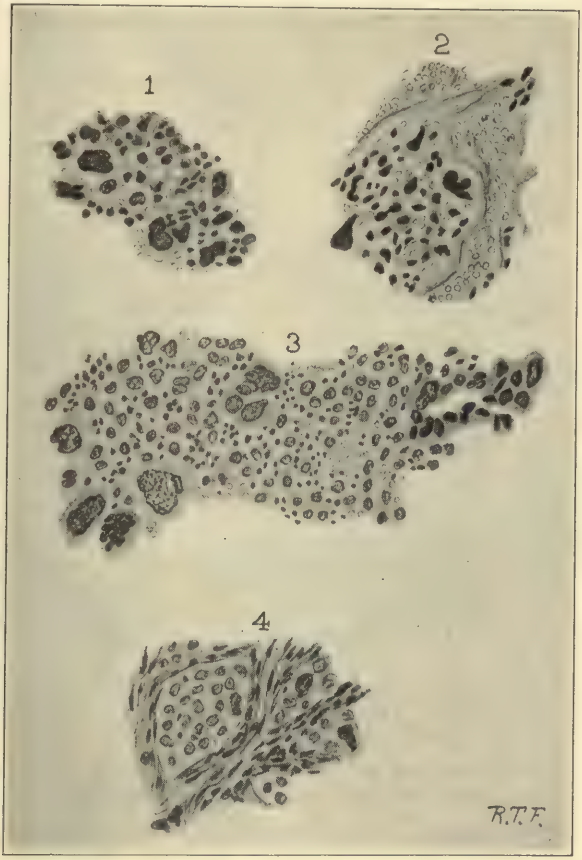

FIG. 208.—CURETTINGS FROM CANCER OF THE CERVIX. Resembling atypical chorionepithelioma. (Case of Dr. F. C. Wood.) 1. Resembling syncytium. 2. Chorionic wandering cells. 3. Combined syncytium and Langhans' cells. 4. Typically alveolar arrangement of carcinoma showing true nature of the growth.

The majority of these cases in some part of the growth show multiple layers and frank transitions to adenocarcinoma. Clinically these cases are malignant and recur after removal. The recurrences may show typical adenocarcinoma.

Frankl (280) reports a *benign adenoma* of the cervix which resembled thyroid tissue. Figs. 214 and 215 show a section of a cervical tumor in

the writer's possession (no clinical data are available), which appears to be a benign adenoma.

Haultain (281) reports a simple *papilloma* of the corpus uteri. The warty growth was covered with a simple layer of cylindrical epithelium upon a fibrous connective tissue base. No signs of infiltration existed.

Less differentiated forms are the *typical "adenoma malignum"* with glands arranged without order, placed back to back and with tortuous worm-like convolutions. The lining epithelium is irregular, may be in multiple layers, projects into the lumen or penetrates the membrana propria, growing

FIG. 209.—SQUAMOUS CELL CANCER OF THE CERVIX. (Low power.) Cut on "the flat." Showing transverse section of papillae. (Vascular connective tissue surrounded by ill-defined epithelial covering.) Superficial resemblance to perithelial sarcoma.

into the stroma. Irregularity of size of the nucleus and other atypical cell characteristics as in cancer are evident.

Next is *adenocarcinoma* in which the glands may still be well imitated (Figs. 216 and 217), or the alveoli be crowded and the lumen almost obliterated (Figs. 218 and 219). Finally, forms in which an origin from either cylindrical cell or squamous type may be claimed (Fig. 220), complete the transition (carcinoma simplex).

Squamous or cylindrical types, alike, may form either exophytic (vegetative or papillary) or endophytic (infiltrating) tumors. Clinically no regular variation of malignancy can be associated with any type of cell.

Origin from "erosion glands" and ectropionated mucosa are often claimed for cylindrical-celled cancers of the portio. The writer declines to enter upon this much debated question as our "knowledge" is entirely based upon surmise.

Cytology.—Obata (l. c. 277) gives an excellent survey of certain details of the cytology of uterine cancer.

Giant cells, mainly polynuclear in type, were found in 29 of 134 solid cancers, and in only 3 of 112 glandular types. *Glycogen* was found 9 times

FIG. 210.—SECTION FROM AN INFLAMED CERVIX. (Low power.) Passing through junction of corium and papillae of the epithelium. This section was diagnosticated as a cancer. Note regular concentric arrangement of pseudo-alveoli, absence of polymorphism and resemblance to surface epithelium. At " 1 " the section strikes epithelium at right angles to surface.

in 69 cancers; *mucin* occurred only in glandular types, 8 times in 112 cases. New formation of vessels was uncommon. Cancer cells in the lumen of blood vessels were found 11 times—twice in arteries. Central necrosis of cancer alveoli was noted in over 30 per cent of solid types.

The stroma is not only passively involved, separated, substituted and destroyed by epithelial elements but in cases of cauliflower growth increases and proliferates. Mitoses are rarely found. Elastic fibers persist around the blood vessels and in the preformed stroma, but no new formation takes

place (McConnell, 282). The cell spaces (alveoli) are outlined with white fibrous tissue, but no intercellular network exists (White, 283). The main part of the stroma is white fibrous tissue.

A tissue reaction is commonly set up at the periphery of a carcinoma. According to Obata (l. c. 277) it was absent only 4 times in 134 cases of solid cancer, and present only 17 times in 112 glandular ones. The infiltration which may be composed of polynuclear leucocytes in cases of infected breaking down growths, is more regularly lymphocytic, often also containing plasma cells, eosinophiles and mast cells. It has been interpreted as

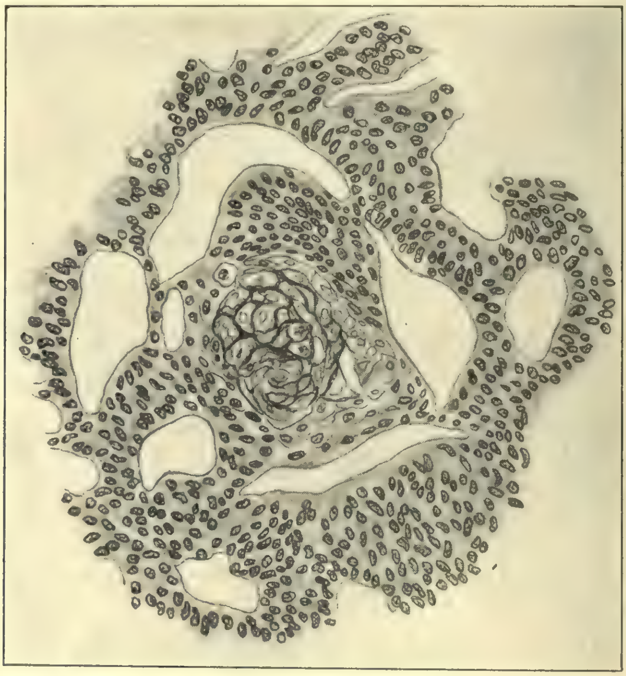

FIG. 211.—ADENOCARCINOMA OF THE CERVIX. (Medium power.) (C. Solidum.) Secondarily glandular according to the classification of Schottländer and Kermauner. In the center is a pearl with beginning cornification. Throughout, the indication of glandular structure is evident.

due to infection, to cancer toxines or a purely foreign body reaction. See Fig. 221.

Degeneration of the stroma may occur. Hyaline degeneration, especially of or near blood vessels, is frequent (Fig. 222). Mucoid changes and calcifications have been noted by Schottländer and Kermauner (l. c. 190a, p. 491).

The endothelium of the small and middle-sized blood vessels often proliferates as in granulation tissue.

Degeneration in the epithelial elements commonly takes the form of cornification. Hyaline degeneration, which produces diffusely staining

areas, and necrosis, especially of the central contents of alveoli, also occurs (Figs. 221 and 223).

So-called *mucoid adenocarcinoma of cervix* has been described by Miller (284), who also collected five cases from the literature.

The alveolar lumina were distended with mucus. Meyer-Wirz (285) reports a case in which the mucus secreted by the cervical cancer was dis-

FIG. 212.—"ADENOMA MALIGNUM" OF THE CERVIX. (×10.) Case of Dr. F. C. Wood. Shows infiltration of the cervical canal as in ordinary carcinoma of the cervix. Cervical canal to left, cervical wall to right.

charged into the retroflexed (later distended and incarcerated) corpus uteri, a simple adenocarcinoma of the corpus coexisting. Whether this gelatinous type of carcinoma is less malignant than other cervical cancers is a debated question.

Calcification in the form of psammoma particles is of occasional occurrence (Wells, l. c. 219; Steida, 286). Calcification of larger areas has been reported by Cullen (l .c. 66). The deposit usually occurs in solid (squamous portions) of a cancer.

CARCINOMA OF THE UTERINE BODY

Corporeal, Fundal.—AGE DISTRIBUTION.—Peterson (l. c. 206) in 94 cases found the maximum number of cases (26.5 per cent) between 55 and 60 years; 46.7 per cent being between 50 and 60 years. This is 15 years later than in his cervical cases. Of Koblanck's (l. c. 207, p. 672) 283 cases 50 per cent were in this same decade. Bland Sutton (287) found a corporeal cancer in a woman of 84 years. The youngest woman in Peterson's series was 22 years old.

INFLUENCE OF PREGNANCY.—This is less marked than in cervical cancer. Among Theilhaber's (l. c. 184) cases of carcinoma corporis, 27.5 per cent

FIG. 213.—MEDIUM POWER OF FIG. 212. "ADENOMA MALIGNUM" OF THE CERVIX. Note the irregular and close packed distribution of glands lined by a single layer of epithelium. This tumor recurred after amputation of the cervix.

were nulliparae; Deelmann (l. c. 212) found 6 times as many nulliparae among cases of corpus carcinoma, Goebel and also Fast (quoted from Deelman) finding the percentage even higher. Levine (l. c. 187, Table V) concedes double the percentage of corpus cancer in the nulliparous, but in women that have borne children, finds an equal percentage. Cullen (l. c. 66) found 52 per cent of 19 cases of corporeal cancer nulliparous: Wilson's figures in 56 cases being 50 per cent (l. c. 241).

FREQUENCY OF OCCURRENCE.—About 10 to 15 per cent of uterine cancers occur in the corpus, according to most statistics.

In 500 cases Peterson found 94, or 18.8 per cent, cancers of the body; Koblanck, in 6354 cases, only 4.4 per cent; Wilson (l. c. 241, p. 449) in 596 cases, 11.2 per cent, while Wertheim's clinic (Weibel, 287a) saw only 70 corporeal to 1500 collum cancers (0.46 per cent).

TRAUMA.—While injuries of the cervix have been considered *precancerous conditions* in carcinoma colli, fibromyomata and polypi are so regarded by various authors in corporeal carcinoma.

FIBROMYOMATA.—Noble (288) found corpus carcinoma more numerous than cervical cancer (75 to 63) in nearly 5000 cases of fibroids collected from the literature. Williams (289) finds them in 1.4 per cent of his 700

FIG. 214.—DIFFUSE ADENOMA OF THE CERVIX. The tumor is too diffuse and widespread to be ascribed to fetal rests, to which it bears a superficial resemblance. 1. Muscle fibers of cervix. 2. Group of glands (see high power Fig. 215.) 3. Similar glands cut longitudinally. 4. Blood vessel. 5. Normal cervical glands. 6. Cervical surface epithelium.

cases. Adenocarcinoma is at least more common in association with fibroid tumors, rising from 17 or 18 to 100, to 100 to 30. According to Hertel (290a), it is four times as frequent (Fig. 224).

The association with *uterine polyps* has never been subjected to numerical study. It has been repeatedly noted in beginning carcinoma (Mortier, 291), the tip of the polyps showing carcinoma, the base being still benign.

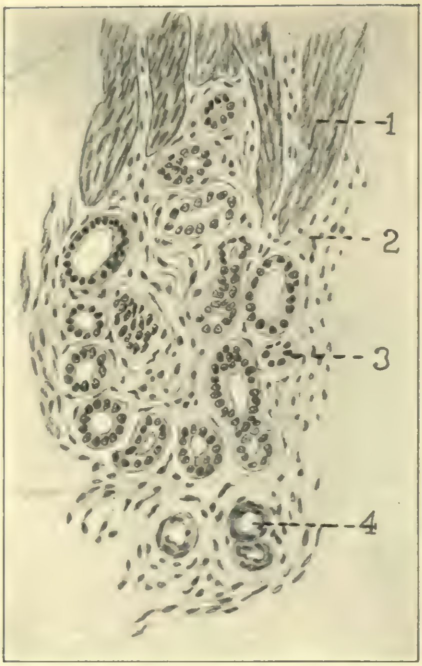

FIG. 215.—MEDIUM POWER OF FIG. 214. ADENOMA OF THE CERVIX. 1. Muscle fibers. 2. Connective tissue of cervix. 3. Transverse section, adenomatous glands, lined by low cubical epithelium, occasionally ciliated, with no distinct basement membrane. 4. Small blood vessel.

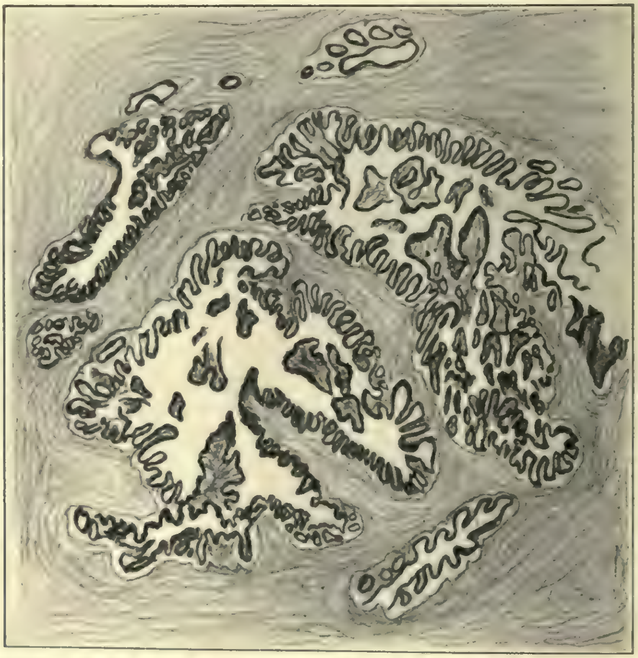

FIG. 216.—ADENOCARCINOMA OF THE CERVIX. (Very low power.) Note large glands with papillomatous projections producing labyrinthine interlacings.

A case of corpus cancer, arising at the site of irritation produced by a douche nozzle left in the uterus for two years, is of interest (Soubreyan and Peyron, 291a).

MACROSCOPIC APPEARANCE OF CORPUS CANCER.—The tumor may appear as a circumscribed polypoid (Fig. 224) or sessile growth, or as a

FIG. 217.—HIGH POWER OF FIG. 216. Shows the many layered epithelium with small fairly regular nuclei. Due to poor fixation the epithelium has shrunk away from the surrounding connective tissue.

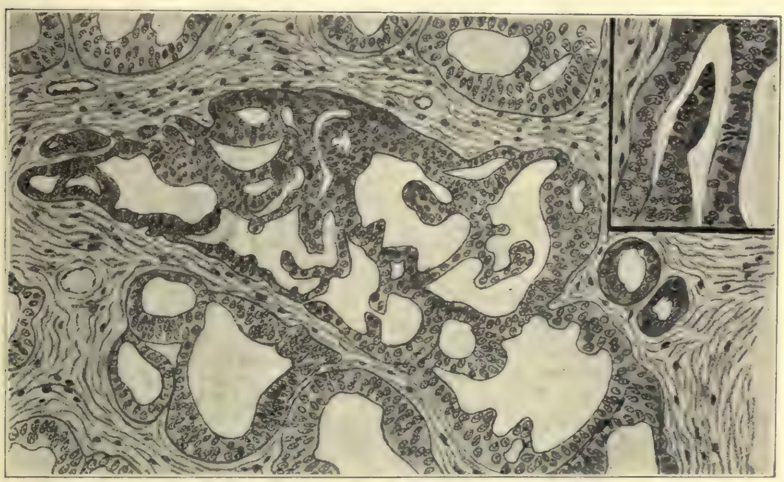

FIG. 218.—ADENOCARCINOMA OF THE CERVIX. (Medium and high power.) Marked irregularity of alveoli with fusion of neighboring glands. More marked polymorphism of the nuclei. Resemblance to cervix epithelium is lost.

diffuse infiltration (Gessner (292) 22 to 14) (Fig. 225), rarely as a surface process on the mucosa ("Zuckerguss," Schaunenstein, l. c. 188).

Exophytic growths may remain limited to the surface of the mucosa for a long time; eventually, however, they penetrate the musculature. The diffuse growths are endophytic from the outset and while the uterine cavity

may be filled by friable white to yellow masses, the musculature is penetrated more and more deeply until subserous bosses develop on the peritoneal surface.

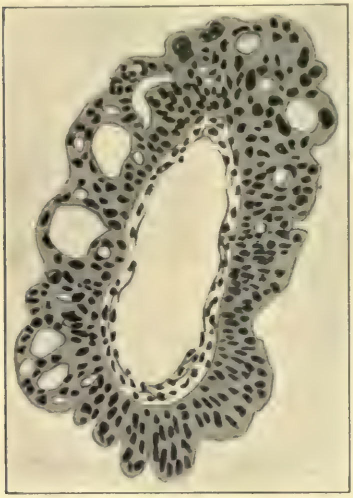

FIG. 219.

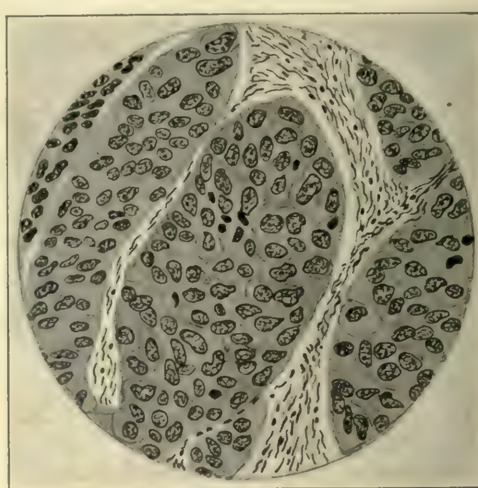

FIG. 220.

FIG. 219.—ADENOCARCINOMA OF THE CERVIX. (High power.) A surface papilla struck transversly showing polymorphism of epithelium with fenestration. Delicate central connective tissue core.

FIG. 220.—SOLID CARCINOMA OF THE CERVIX. (Transition type.) Conforms to typical medullary cancer (carcinoma simplex).

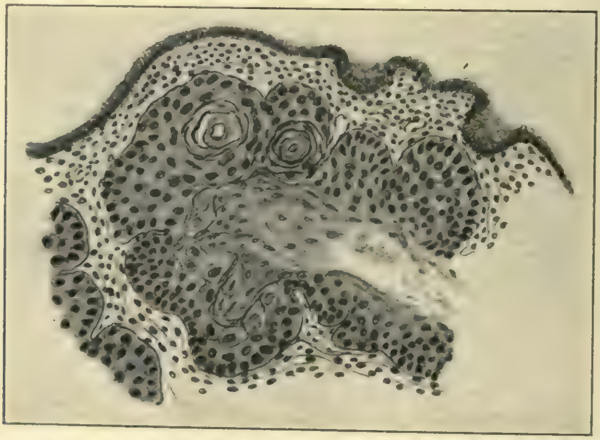

FIG. 221.—SQUAMOUS CELL CANCER OF CERVIX. (High power.) Alveolus seen underneath intact columnar epithelium of cervix (above.) Marked round-cell infiltration of connective tissue. Central degeneration of cancer cells within alveolus.

Spontaneous perforation into the peritoneal cavity has been reported by Weil (293) and Cullen (l. c. 66, p. 413). Instrumental performation may

be hard to avoid as in Schottländer and Kermauner's case 116 (l. c. 190a, p. 469), in which a senile atrophic uterus failed to hypertrophy when its cavity was distended by the new growth. For literature see Ballard (293a).

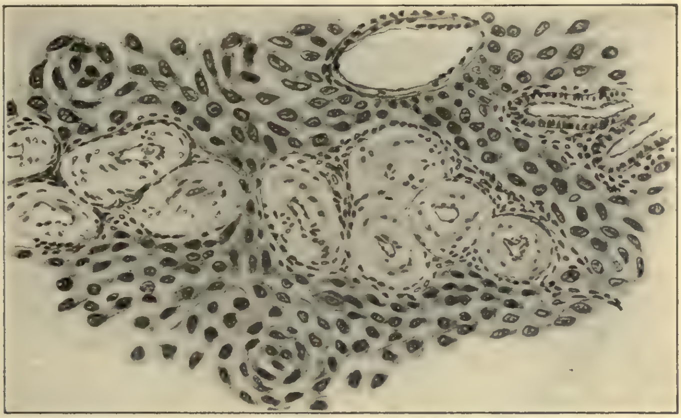

FIG. 222.—SQUAMOUS-CELL CANCER OF THE CERVIX. (Medium power.) Solid areas of cancer epithelium surrounding in center blood vessels with hyaline degeneration of vessel walls. To the right, well-preserved cervical glands.

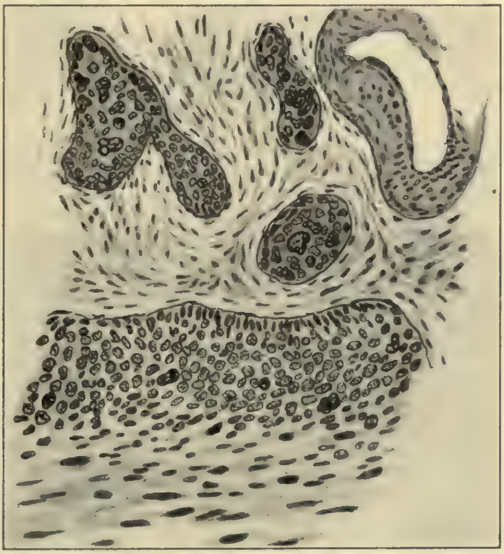

FIG. 223.—POLYMORPHOUS ALVEOLAR CARCINOMA OF THE CERVIX. (Medium power.) Note above, marked difference in size of cells, chromatin irregularities, progression along perivascular lymph spaces. At bottom large alveolus with central degeneration producing resemblance to sarcoma.

Gebhard (l. c. 31, p. 151) classified carcinoma corporis into c. tuberosum, papillare, villosum, according to the surface appearance, a purely descriptive classification. Fig. 224 shows a polypoid, Fig. 225 a diffuse adenocarcinoma.

The diffuse growths show greater tendency to invade the collum and from there to extend to the parametria, but Schottländer and Kermauner's series of 17 cases in which only 6 were limited to the corpus (l. c. 190a, p. 463) shows an unduly high proportion.

FIG. 224.—UTERUS CUT OPEN SHOWING FUNDAL FIBROMYOMA. (×½.) Polypoid "adenoma malignum" of right tubal angle, and also below to the left of this, a small submucous polyp of the endometrium.

FIG. 225.—DIFFUSE ADENOCARCINOMA OF THE CORPUS. (×⅓.) Involving the entire corporeal endometrium in the shape of smooth excrescences.

As the tumor mass increases in size its nutrition suffers, producing necrosis and breaking down of the surface. Hence, though to a less degree than in cervical cancer, stinking craters may develop.

Being inaccessible to the eye the diagnosis of corporeal cancer is difficult.

Appearance of bleeding after the menopause, watery or bloody discharge and enlargement of the uterus are suspicious. The diagnosis must be confirmed by exploratory curettage. As the course is slow, many cases are recognized while still in an operable stage.

Duration is double as long or longer than in cervical cancer, according to Wilson (l. c. 241, II, p. 533) up to 2 to 4 years.

Termination.—Corpus carcinoma has a tendency to remain localized much longer than the cervical cancer. Erosion of the uterus is followed by extension to the cervix, tubes or ovaries and peritoneum. Vaginal metastases are uncommon (Fischer, 294), Cullen (l. c. 66, p. 414). Eventually the parametria are infiltrated and the entire pelvis becomes a solid tumor mass.

In far advanced cases it is impossible to distinguish the point of origin of the tumor. Earlier involvement of the peritoneum occurs in corporeal growths and hence peritoneal dissemination and matting of the intestines are frequent. The autopsy reports on page 286 apply as well to corporeal as to cervical growths.

Williams (294a) mentions a utero-intestinal fistula found at autopsy.

Extension to Adjacent Organs.—In all his operable cases Cullen saw no case of extension to the tubes and ovaries (l. c. 66, p. 437).

The literature, however, contains numerous instances, Löhlein (295), Reichel (296), Ries (297). At autopsy coincident involvement of corpus uteri, tubes and ovaries are common. It may be impossible to recognize the primary focus. Extension along the lumen of the tube (Milner, 298), free tumor particles in the uninvolved tubal lumen (Sitzenfrey, 299), along the musculature or in the lymph channels (Taussig, 300), have been noted and are mentioned as probable modes of extension.

The *lymph glands* are involved more rarely and later than in cervical cancer, although of 31 cases operated upon in Wertheim's clinic, gland involvement was found in 5, or 16 per cent (Weibel, 287a). Unless the growth is near the internal os the lumbar glands are first affected. The external inguinal glands have also been involved, rarely the iliac group.

Cullen (l. c. 66, p. 431) mentions finding inguinal, pericardial, bronchial, cervical, and perihepatic glands cancerous at autopsy.

Metastases can occur in the ovaries, peritoneum, tubes, vagina, vulva (Offergeld, 301), and other organs in advanced cases. Occasionally the uterine tumor may be well localized but the metastases may be numerous, as in the case of Kaufman (l. c. 125a, II, p. 1031), in which they were found in the liver, lung, kidney, thyroid, both femora and widespread in the vertebral column. The same author reports a large cancerous node in an inguinal hernia sac (l. c. 125a, II, p. 1029).

The pelvic colon contained metastastic growths in 2 of Wilson's 38 cases, (l. c. 241, II, p. 521).

The operability is higher than in cervical cancer. Wertheim (302) found 97 per cent. For statistics see Koblanck (l. c. 207, III, ii, p. 782).

The absolute *cures* of Wilson (l. c. 241, II, p. 533) were 24 per cent; Wertheim had 51 per cent free from recurrence for 5 years or over, Cullen 60 per cent (some cases operated upon only one year).

Recurrences, as is evident from the preceding, are less frequent than in cervical cancer. Weibel (240b), reviewing Wertheim's cases, found that all recurrences appeared within 3 years.

Gland recurrences, lumbar, inguinal, iliac and liver and lung metastases are most common. "Wound implantation" in the perineal scar after Schuchard's incision has been repeatedly reported (Hirsch, 303), Milner, l. c. 298); for true vaginal metastases see Hellendahl (304).

Pregnancy has never been noted in corporeal cancer.

FIG. 226.—COINCIDENT TUBERCULOSIS AND ADENOCARCINOMA OF THE UTERINE MUCOSA. (Medium power.) (Specimen of Dr. Eli Moschcowitz.) The tubercles and the cancer are in close proximity. Both are typical of their kind and apparently unaffected by this rare symbiosis. 1. Tubercles composed of epitheloid and giant cells. 2. Adenocarcinoma breaking through the gland capsule and growing diffusely in the stroma. 3. Normal uterine gland.

Tuberculosis has not infrequently been found coexisting (Fig. 226) occasionally in the tubes and peritoneum, more often in the uterus itself (d'Halluin and Delval (305), Koblanck (l. c. 207, III, ii, p. 675) 6 cases from literature).

Pyometra (see page 284) occurred 4 times in 38 cases of Wilson's (l. c. 241, II, p. 542). *Hematometra* and colpos was reported by Sondheimer (306) in a woman of 67 years, a one para. There were 3 liters of fluid.

Secondary and Metastatic Corporeal Cancer.—As previously mentioned, cervical carcinoma may spread by continuous or discontinuous (lymphatic) growth to the corpus and there form discrete or diffuse tumors in the musculature or in the mucosa (Seelig, 307) (Fig. 227).

Metastatic carcinoma is commonest from ovarian growths, Gasarbekian (308) 12 cases, Offergeld (309), Studdiford (310). It has occurred after tubal cancer (v. Franqué (311), Knoop (312), bronchial (Chiari, 313). Roger Williams in 3 per cent of 167 post mortems of breast cancer found metastases on the peritoneal surface of the uterus; Couvelaire (314) during pregnancy noted stomach cancer with uterine metastases.

Multiple cancers in the uterus have proved a fruitful source for discussion. Two types might be found, the first a simultaneous growth of two

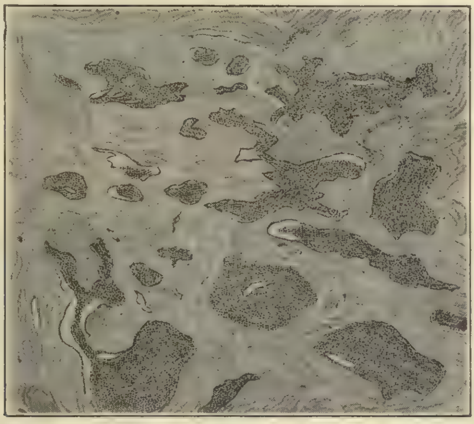

Fig. 227.—Secondary (metastatic) carcinoma of the uterus. (Low power.) The cancer has spread along the preformed spaces, producing a peculiar marbled appearance. Some of the clear spaces appearing at the side of or within the cancer alveoli are partially lined with endothelium.

carcinomata of different type (as adeno and squamous) no such case being on record, and secondly, two independent cancers (cervical and corporeal) of the same histological type, but separated by a large zone of normal uterus. Of this latter class, a number are on record.

Winter (l. c. 32, III, ii, p. 624) has collected twelve cases of which he classifies five as primary cervical secondarily corporeal, two as primary corporeal, and five as accidental coincidences. Cullen (l. c. 66, p. 592) analyzes several of these cases, deciding that none of them are conclusive. Cases like Gellhorn's (315) are due to continuous growth involving both divisions of the uterus.

Schenk and Sitzenfrey (316) report simultaneous cancer of the stomach, ovaries and uterus, Tate (317) coexistence of ovarian, cervical and corporeal cancer. Unquestionably such combinations are the result of secondary deposits from one source.

Carcinosarcoma is discussed on page 258.

Complete removal by the curette of adenocarcinoma of the fundus has been repeatedly reported, with freedom from recurrence up to four years. Ladinsky (318) collected 22 cases including three of his own. The mechanism is demonstrated by cases in which curettage was followed by hysterectomy and only minute portions of tumor were found remaining. Frank (319); Wiener (320), (Fig. 228).

Carcinoma has occurred in *malformed uteri*, especially in accessory horns—Vineberg (321), Buist and Valentine (l. c. 260), Melson (l. c. 258). Adenocarcinoma of the fundus is the type found.

Uterine stones, perhaps resulting from calcified myomas, have been noted in cancer of the fundus by Cullen (l. c. 66, p. 411). For literature see Thorn (322).

Histology.—Cylindrical Cell Cancer.—The frequency of glandular types in the corpus has been stated on page 288.

What has been said concerning cylindrical cell cancer of the cervix applies as well to the corporeal growths. *Adenoma malignum* or *destruens* (Fig. 229), *adeno carcinoma* (Figs. 230 and 231) and *solid cancer* of medullary (Fig. 232) or, more rarely, scirrhous types are noted.

These varieties may be found as nodular, polypoid, papillary or villous growths. The numerical occurrence of various histological types according to Obata (l. c. 277), was as follows:

	Corpus	Cervix
Adenoma malignum with one cell layer...	9	3
Adenoma malignum with multiple layers..	29	5
Secondarily solid (i.e., adenocarcinoma)..	11	3
Mainly adenocarcinoma...............	32	5
Equal parts solid and adeno............	7	–

Squamous-cell cancer is uncommon in the uterine body. Obata (277), of 134 primarily solid cancers, found only 11 corporeal, although his material (because of many curettings sent from outside sources) shows an unduly high percentage of corporeal neoplasms.

The typical squamous-cell cancer resembles that found in the cervix and elsewhere. It may be preceded by changes in the surface epithelium (see ichthyosis or psoriasis uteri, p. 185). Eventually the uterine glands disappear.

Gebhard (l. c. 31, p. 148) reports two cases in which in cervical cancer a squamous-cell surface growth spread over the entire corporeal mucosa, without showing great invasive tendency, apparently a transition between ichthyosis and the "zuckerguss" type of cancer (Benckiser, 322a). Emanuel and Gellhorn's cases, likewise, had cervical involvement but were penetrating the muscle (322b). In Norris' case (323) the cervix was

FIG. 228.—PHOTOMICROGRAPH OF ADENOCARCINOMA OF THE UTERUS, almost completely removed by curettage. Good example of transition between adenocarcinoma and "adenoma malignum."

FIG. 229.—"ADENOMA MALIGNUM" OF THE CORPUS UTERI. (High power.) Photomicrograph difficult to distinguish from normal closely packed glands. Such close juxtaposition under physiological conditions should be accompanied by marked secretory phenomena or if due to stationary hyperplasia should show more interglandular tissue.

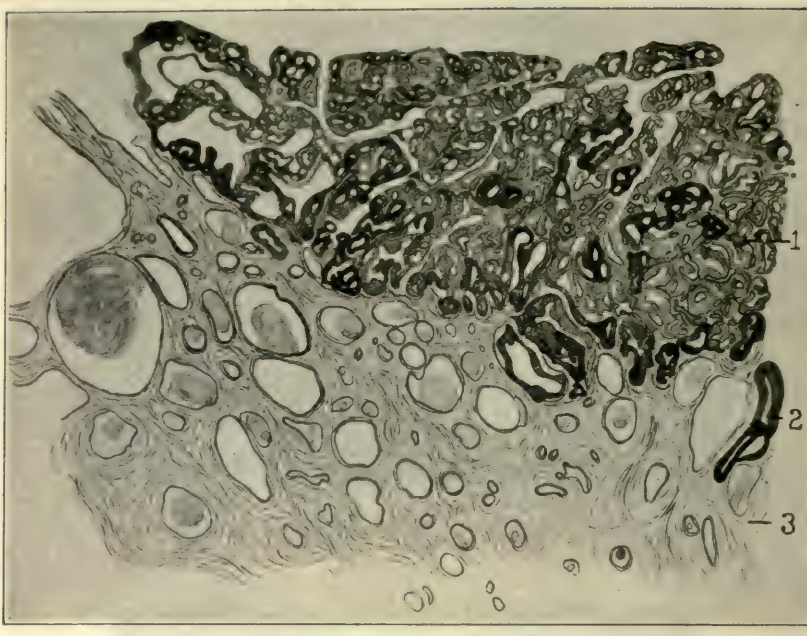

FIG. 230.—ADENOCARCINOMA OF THE UTERUS SHOWN AT JUNCTION WITH CYSTIC ENDOMETRIUM. (Very low power.) Note sharp demarcation between the endometrium and the cancer. 1. Carcinoma. 2. Advanced posts of cancer. 3. Endometrium.

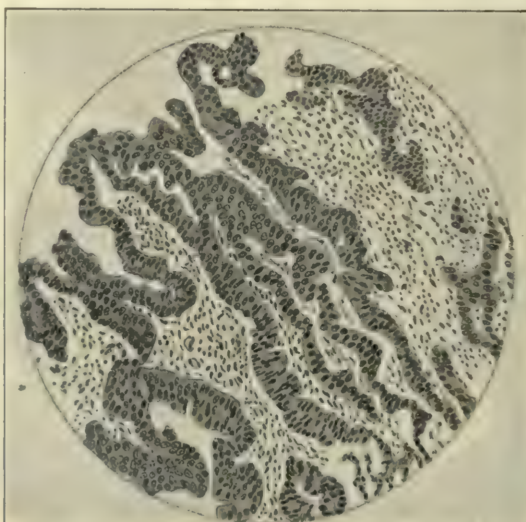

FIG. 231.—ADENOCARCINOMA OF THE UTERUS. (Medium power.) Showing lawless arrangement of glands (rain-worm like), variation in size and type of the nuclei.

normal. Pyometra has been repeatedly noted in these cases (Flaischeln (324), and may produce the squamous change initiating the cancer.

Transition types, especially such as show adenocarcinoma with areas of squamous cells, cornification and even pearl formation are not uncommon (Frank (325), Ivens (326), Fig. 233). Such changes are due to metaplasia of the cells, perhaps resulting from changes in nutrition.

A combination of adenocarcinoma and epithelioma supposedly separate tumors, were reported by Kaufmann (l. c. 125a, II, p. 1034), Emanuel (l. c. 322b), Hofmeier (327). Probably their origin must be referred to more marked metaplasia than in the types just described rather than to two separate cancers.

Albrecht (328) has reported a *mucinous adenocarcinoma* originating in the corpus, infiltrating the cervix and parametria, with widespread glandular involvement (including thoracic).

FIG. 232.—SOLID CARCINOMA OF THE UTERINE BODY. (Very low power.) Typical brain-like convolutions separated by preëxisting muscle bundles. In many spots, due to poor fixation, the cancer has shrunk away from the surrounding musculature.

As in the cervix, psammocarcinoma has been noted (Schmit (329), Schütze, 330). The observation is of no great importance.

Radium Effects on Cancer.—The gross effects which show themselves in melting away of cauliflower growths, restoration of the outline of the cervix, except for tissue actually destroyed, cicatrization and epithelialization require no further description here. For clinical details see Discussion, American Gynecological Society (331).

Histologically, cessation of mitotic division, etc., is the earliest effect, next appears nuclear vacuolation, the cell body and nucleus staining more diffusely (Fig. 234). Finally cell detritus, fibrin and amorphous material predominate. Lymphocytes and plasma cells appear and eventually a

replacement fibrosis converts the area into scar tissue, Frank (332), Gudzent and Levy (333), Klein and Dürck (334), Alter (332).

Diagnosis.—Cervix.—The macroscopic diagnosis really falls into the rubric of books on gynecology. Because of its extreme importance an outline will be given here. See Winter (l. c. 203) and also Cullen (l. c. 66, p. 476).

Suspicion is aroused by *eversion* and *erosion* (p. 198) because of pouting red, granular or fissured appearance, bleeding on trauma; absence of induration and friability. Microscopic characteristics, see page 199. *Ulcer* from trauma or prolapse with granulating area; at times slight induration,

Fig. 233.—Adenocarcinoma of the uterus with metaplasia into squamous cancer. (Medium power.) Below and to the right is glandular carcinoma of the type of "adenoma malignum." Above and to the left sheets of squamous epithelium occur still showing evidence of glandular arrangements. The metaplasia is probably due to nutritional causes.

see page 202. *Hypertrophy* of cervix due to edema, dilated cervical glands (nabothian follicles). *Polypi* projecting from cervix either of cervical or uterine origin, may be sloughing, see page 266. *Condylomata,* especially in pregnancy, may produce foul discharge, see page 148. *Syphilitic ulcers,* see page 208; tuberculosis, page 205. Other tumors such as cervical fibroid (non-ulcerating), sarcoma, endothelioma or adenomyoma require histological examination to assure differentiation.

The microscopic characteristics of all the foregoing are sufficiently distinct to permit of differentiation. When only small particles are sent for diagnosis it will be noted before they are placed in hardening fluid, that cancer is usually opaque, hard, friable and granular; sarcoma soft, brain-

like and flocculent; endometrium (especially if fungoid) mucoid, glairy and transparent, Kaufmann (l. c. 125a, II, p. 1036). Atypical epithelial proliferations, which are the most fruitful sources of error, have been discussed on page 268.

Corporeal.—Grossly in the removed uterus, fibromyoma, adenomyoma, sarcoma, chorionepithelioma, polyps, fungoid and hyperplastic endometrium, placental rests and tuberculosis come into question.

In curetted material the microscope must decide. It is well to keep in mind that areas of thickening and changes into squamous epithelium of the uterine surface epithelium, are rare except in acute adnexal disease (p. 185), tubercular endometritis (p. 204), and in senility (p. 38). Occasionally the

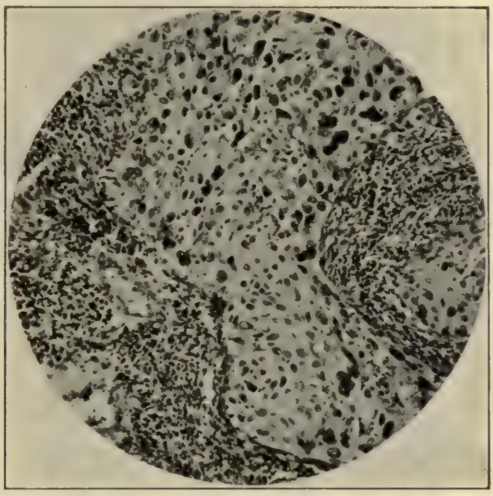

Fig. 234.—Photomicrograph, squamous-cell cancer of the cervix. Showing pyknosis, vacuolation and diffuse staining as the result of one thousand milligram hours of radiation with radium, 8 days previously.

curette mixes squamous epithelium from the portio in with corporeal mucosa (Fig. 235). The uterine glands may extend into the musculature without signifying malignancy (Fig. 236). Placental rests are recognized by the villi (p. 464); if villi are absent decidual islets may give an epitheliod appearance (Fig. 136). Decidual cells in the muscle resemble sarcoma; they lie in the long axis of the musculature. The decidua of extra-uterine pregnancy and the premenstrual phase (p. 447), although it shows marked pseudopapillation of glands shows normal arrangement of glands and epithelium (Fig. 70), no "rain worm" like convolutions (Fig. 231) such as are found in adenoma malignum and no mitotic irregularities. At times it is impossible to make a diagnosis with the material on hand (Fig. 238).

Poor hardening, thick sections, recourse to the high power of the microscope without orientation increase the liability of error.

Chorionepithelioma of Uterus.—See page 471 under Pregnancy.

Hypernephroma occurs rarely as a metastasis in the uterus (Hertz, Hartmann, 334b).

Hodgkin's disease produces lesions in the uterus which might be mistaken for a round-celled sarcoma (Jessup, 335).

FIG. 235.—UTERINE CURETTINGS CONTAINING FRAGMENTS OF SURFACE EPITHELIUM. (Medium power.) Such structures are frequently found in uterine curettings and may mislead. 1. Papilla of cervical mucosa in cross and oblique section. High columnar epithelium with basal nucleus upon a connective-tissue stroma. Resembles villi of the chorion. 2. Squamous epithelium from portio often mistaken for carcinoma. Regular distribution of the cells showing darker basal cells and lighter superficial layer. 3. Normal uterine mucosa with dark nucleus in the middle of the cell body. 4. Cervical glands with high columnar epithelium. 5. Giant cell-like bodies resulting from the section passing through the tip of a cervical papilla. 6. Disconnected strips of cervical epithelium at times mistaken for "adenoma malignum."

Schlagenhaufer (l. c. 132a) reports a *chloroleukemic infiltration* of the uterus involving cervix, endometrium, myometrium and peritoneal coat, and also the ovaries. The tissues appeared green. The infiltrate consisted of large mononuclear leucocytes.

PARASITES

Parasites are of rare occurrence.

Ecchinococcus usually is only secondary in the uterus, growing toward this organ from the subperitoneal pelvic connective tissue (v. Kroph (336), Gussakow (in pregnancy), 337).

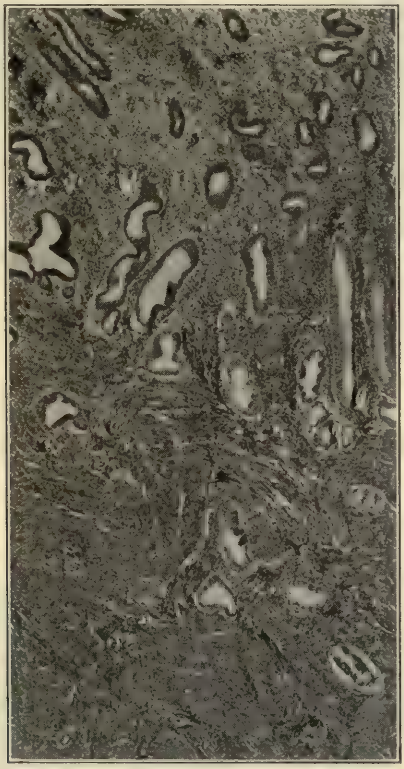

FIG. 236.—PHOTOMICROGRAPH SHOWING "INVASION" OF UTERINE GLANDS INTO THE MUSCULATURE. This condition is non-malignant, in some instances being due to inflammation, in others being an artefact resulting from the wavelike junction of mucosa and musculature.

Turenne (338) describes a primary (?) cyst in the anterior uterine wall, no other focus being discoverable. He has collected eleven cases from the literature. Of these several ruptured into the uterine cavity and expelled their contents per vaginam.

Gaifami (339) describes a *leech* entering the cervix during a bath.

Salzer (340) found *trichinae* in the placenta, but not in the uterine wall.

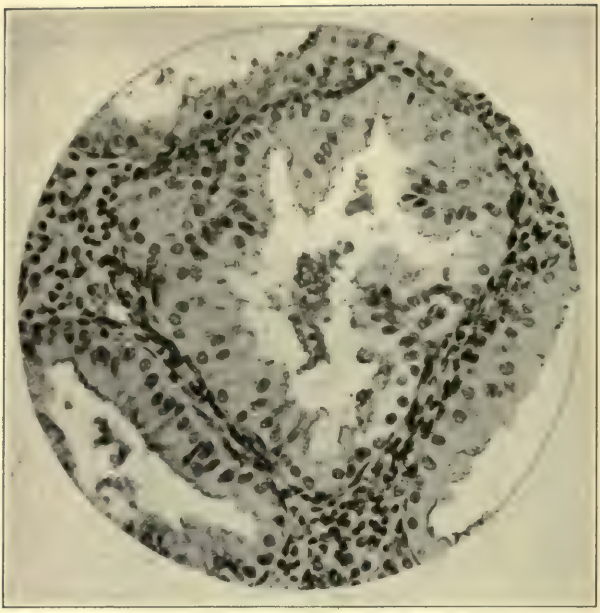

FIG. 237.—NORMAL UTERINE GLANDS IN THE SECRETORY STAGE. Photomicrograph (High power.) The irregular lumen, the pseudo-papillary projection produce a faint resemblance to adenocarcinoma.

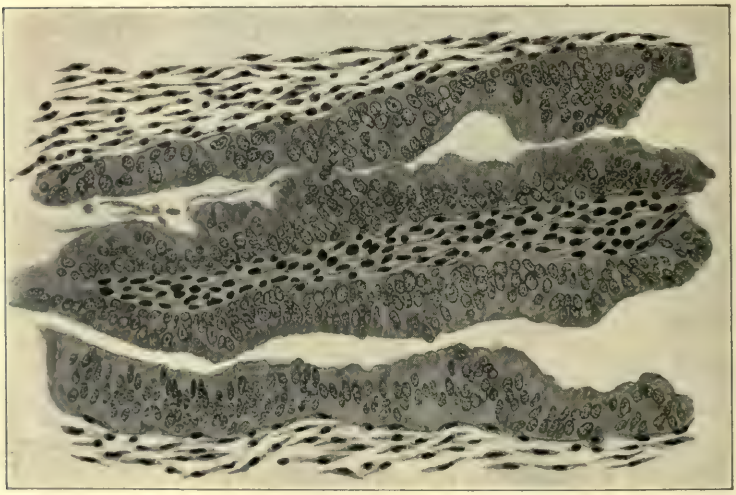

FIG. 238.—CURETTINGS FROM A WOMAN OF 57 YEARS WITH INCREASED MENSTRUATION. From five blocks cut almost in serial section, this small area was the sole suspicious portion. Repeated subsequent curettings showed absence of malignancy. Later no evidence of malignancy developed.

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CHAPTER IX

FALLOPIAN TUBES

CIRCULATORY DISTURBANCES

Primarily non-inflammatory conditions can produce hyperemia, engorgement, hemorrhage, and necrosis of the fallopian tubes. They include:

Stasis from general causes such as result in pulmonary and portal obstruction (heart, liver and pulmonary disease) and asphyxia neonati (Martin, 1).

Infectious diseases such as measles, scarlatina, smallpox and cholera (Fraenkel, 2) and the hemorrhagic diatheses (purpura) in which hemorrhage into the lumen and tissues of the tube also occurs (Rusi, 3).

Phosphorus poisoning (Martin, l. c., 1, p. 78).

Local obstruction resulting from *traction of tumors* such as fibroids of the uterus, torsion of even normal adnexa (Norris, Rüder, 4) or by ovarian tumors with twists of their pedicle, more rarely tumors of the fimbriae (Herde, 5), by inversio uteri (Hennig, 6) and by strangulation in hernial sacs (Léjars, Heineck, 7).

Thrombosis of the spermatic vessels, too, may produce hyperemia, etc.

In all these lesions the very vascular walls and mucous membrane of the tube show swelling and engorgement with consequent blue-black color. The fimbriae are erect and pouting. Later, hemorrhage into the lumen and into the muscularis (apoplexia) takes place. Eventually hemorrhagic necrosis may occur (Saenger (8), Schottländer, 9). Adhesions regularly form, which may shut off the ostium from the general peritoneal cavity.

Rupture into the intestine and bladder are on record (Henning l. c. 6), in typhoid fever, although here a bacterial infection must be considered. If necrosis occurs, bacterial invasion takes place secondarily.

In spite of its sheltered position hemorrhage from laceration of the tube is reported by Ellsworth and Freeman (9a). In the latter case indirect trauma due to vaulting a fence was given as the cause.

The microscopic appearance of hyperemia shows dilated blood vessels in all the layers of the tube. When hemorrhage takes place extravascular red blood cells are found, and leucocytes in varying number. Later these latter take up blood pigment. The tubal folds are thickened. If necrosis occurs through complete circulatory obstruction, the tissues show less and less affinity for stains and hyaline, acellular areas are noted. In the tubal lumen chocolate-colored, uncoagulated blood is found.

Inflammatory conditions from the outside such as peritonitis cause hyperemia, engorgement and edema, hemorrhage and adhesions. Similar changes result from infections from within the tube. Both conditions will be discussed later.

Hematosalpinx forms whenever, after the uterine and especially the peritoneal ostium is shut off, blood from any source is poured into the tubal lumen. In contradistinction to what is seen in tubal gestation the blood does not clot in hematosalpinx. Often the ostium is open when the hemorrhage begins, but is gradually shut off, as a peritubal hematocele forms. For mechanism of closure see p. 335.

In addition to the sources of hemorrhage mentioned in the preceding paragraphs (Stark, 10), hematosalpinx forms as the result of *gynatresias* from damming back of uterine menstrual blood (Fuld, 11).

The walls of a hematosalpinx may be paper thin (especially when hemorrhage takes place into a hydrosalpinx) or thick. In the latter instance marked fibrosis and disappearance of the musculature is not uncommon. The tubal folds may be unaffected. As the distention increases the folds are smoothed out. The epithelium grows lower. The tubal walls show blood imbibition.

Hematosalpinges may undergo torsion (v. Herff, 12), double torsion (v. Guérand, 13) and infection, or very rarely become profluent into the uterus and vagina (Thorn, 14). Perforation of hematosalpinx due to gynatresia, as a result of trauma or after operative interference (incision of imperforate hymen), with consequent fatal peritonitis was not uncommon (Fuld, l. c. 11).

The writer recalls a case of double genitalia with hematocolpos-metra and salpinx of one side. The patient was operated upon by a general surgeon who, contrary to advice, incised the imperforate hymen without first exploring the hematosalpinx. Within twelve hours death resulted from hyperacute peritonitis with terminal temperature of 109°.

CHANGES IN SHAPE, POSITION, PATENCY, ETC.

The tube is elongated, distorted or flattened when ovarian, parovarian or uterine tumors develop intraligamentously. Payr (15) describes a tube reaching 76 cm. in length (parovarian cyst). The lumen usually remains patent. (See Fig. 331, p. 491.)

Uterine displacements produce tubal displacement and distortion secondarily (in consequence of prolapse, retroflexion, elevation, inversion, etc.).

The tubes are found in hernia together with the ovary and uterus (Andrews, 16). As a sole hernial content, the tube is rarely found; Léjars (l. c. 7) five crural, three inguinal, five were strangulated.

The tubes are rarely twisted off completely (detachment) through constricting bands and membranes and by torsion (v. Rokitansky, 17). For literature see Ogórek (18), who has collected 97 cases.

After obliteration of the abdominal ostium by inflammation the opening has been successfully reëstablished by salpingostomy (normal pregnancy, tubal pregnancy — McCann, 18a, Gellhorn, 55). Ligation, resection, and even exsection of the tube has been followed by return of patency (Ries, 18b, Leonard, 19). Doederlein claims that 6 per cent of non-success is the rule.

INFLAMMATIONS OF THE FALLOPIAN TUBES

Salpingitis is caused by microörganisms. Chemical, thermal and mechanical insults come into question merely as they may produce a *locus minoris resistentiae.*

Etiologically the gonococcus heads the list of organisms. No reliable statistics as to the exact proportion of gonorrheal cases can be given because the percentages vary according to the source of the material, the technic employed, etc.:

Andrews (l. c. 16)	22.5%
Pankow (20)	43%
Heynemann (21)	75%
Wertheim (22)	82%
Gôth (23)	100%

The streptococcus and staphylococcus are most often recovered from puerperal conditions. The tubercle bacillus is noted in from 8 to 25 per cent of cases (Pankow (20), Williams, l. c., 61) depending upon whether all cases are subjected to microscopic examination. The colon bacillus, pneumococcus (v. Rosthorn, 24), typhoid bacillus (Dirmoser, Galliard and Chaput, 25), bacillus of malignant edema, influenza bacillus (25a) and other organisms have been obtained.

Martin and Orthmann (l. c. 1, p. 163) collected 2078 cases of which 386 were septic (and of these 374 were puerperal in origin) and only 279 gonorrhoic in origin (13.4 per cent).

The *age* incidence is largely a matter of chance. Gonorrheal infections in infancy rarely ascend to the tube (Bidwell (26), child of 6). Tuberculosis has been found at an early age, usually as part of a general genital and often of a miliary tuberculosis. The greatest number of cases develop during the period of sexual activity (gonorrheal and puerperal processes). In the senium tubal infection may complicate myoma and carcinoma of the uterus.

The *route* by which infection takes place in gonorrhea is always ascending through the uterus, mainly, (*a*) *surface growth.* In puerperal processes (post abortum and post partum) (*b*) *lymphatic* ascending infection is the rule. A septic peritonitis may however involve the tubes through the ostia, (*descending*) or through penetration of their serous coats. Tuberculosis, if secondary to peritoneal involvement, follows the same method of spread.

More often it is propagated through the (*c*) *blood stream* (metastatic). Ascending tubercular infection, if it exists, is a curiosity (for literature see Jung, Engelhorn, v. Baumgarten, 27). Direct extension through adherent bowel, especially appendix (Pankow (l. c. 20) 22 per cent) accounts for most colon, typhoid, etc., infections. The ovary may secondarily involve the tube, which may also secondarily be affected by any peritonitis no matter what its origin (as from ruptured gastric ulcer). Mixed infection by several routes may take place (Stone and McDonald, 28).

The direct cause for tubal inflammation is various. Gonorrheal infection of the lower genital tract may exist for long periods before tubal involvement is produced by the puerperium, intra-uterine instrumentation or after a menstrual period.

Pyogenic salpingitis likewise follows instrumentation, puerperium, breaking down of a carcinoma, from appendicitis (Grekow, 28a) or in children without known cause (Riedel, 29). In tuberculosis a generally lowered resistance, besides any of the causes just enumerated may permit localization in the genital tract. Even pyosalpinx can occur in virgins (Bégouin, 29a).

Aschoff (29b) describes salpingitis due to laminaria inserted to produce dilatation of the cervix.

Macroscopic Appearance of Acute Salpingitis.—Both tubes, as the disease is generally bilateral, are congested, thickened and more tortuous. The fimbriae are of brilliant red color, turgescent and seemingly erect. On pressure sanious, mucoid, mucopurulent or thick purulent secretion can be expressed from the abdominal ostium.

Unless the course is foudroyant (as in severe puerperal streptococcus infections in which death may occur in from one to three days and in which a lymphangitis and peritonitis are the main findings) soiling of the pelvic peritoneum by way of the ostium early produces peritubal adhesions, intraperitoneal collection of fluid (seroceles or pelvic abscess) and infection of the ovaries.

Upon splitting open the tube the lumen is found reduced in caliber by the swelling. The mucosa is covered with thick purulent secretion. The classification into *catarrhal* and *purulent* salpingitis has no significance except clinically, as these conditions merely indicate stages and degrees of the same infection.

The changes so far described can regress with complete restitutio ad integrum unless the *perisalpingitis* produces closure of the abdominal ostium, kinks or torsion of the tubes.

Continuation of the process is marked by thickening of the muscular wall (infiltration), by occurrence in some instances of *intramural abscesses* (which later lead to *salpingitis nodosa,* usually isthmical) and, after closure of the abdominal ostium, by a gradual reduction in the virulence of the process with resulting subacute and chronic salpingitis.

The final outcome varies greatly, depending upon the source and virulence of the infection and upon the more or less accidental mechanical conditions resulting, as well as upon the period at which the lesion is examined. Norris (30), in 1070 inflammatory lesions of the tubes examined at the University of Pennsylvania Hospital, found the following conditions; Kelly and Cullen (113a), dealing with myomata of the uterus, found the following tubal conditions (934 myomata);

Norris		Kelly and Cullen
151	salpingitides	48
184	perisalpingitides	94
253	hydrosalpinxes	88
425	pyosalpinxes	41
38	tubo-ovarian abscesses	14
19	tubo-ovarian cysts	5

The great preponderance of pyosalpinx in Norris' series is probably due to the fact that this condition most often *per se* creates symptoms necessitating operation and removal.

Chronic salpingitis is characterized by distorted, tortuous, beaded or thickened tubes which are densely adherent to neighboring structures. Changes in the mucous membrane consist of hypertrophy, with obliteration or distortion of the lumen, due to thickening and agglutination of folds (pseudocyst formation). If closure has occurred, the folds become thin and *atrophic* from distention by fluid, which may be serous, purulent or cheesy. The musculature may be hyperplastic; more often the thickening is due to increase of connective tissue (interstitial salpingitis) with atrophy of the muscle elements.

Almost invariably the residua of pelvic peritonitis are evident as peritubal adhesions, producing bound down, distorted and often occluded tubes. The adhesions may be velamentous, or attain great thickness and be indurated and boardlike. Pelvic abscesses, perioöphoritis, oöphoritis and other lesions may be present.

Histology of Salpingitis.—Acute salpingitis is marked by hyperemia of the mucosal folds, infiltration with leucocytes and round cells, loss of cilia by the epithelium lining the tube and exudation into the lumen.

If the process continues, as in gonorrhea and other lesions which do not prove rapidly fatal, the folds of the mucosa appear plump from infiltration and covered with exudate (Fig. 239). Superficial ulcers may develop from loss of epithelium. The infiltration, after the most acute stage is passed, is composed largely of plasma cells and lymphocytes. This led Schridde (31) to conclude that plasma cells infiltration, superficial ulcers and plump folds were diagnostic of gonorrheal salpingitis. Miller (32), Wolff (33) and Gurd (34) have disproved the specificity of these findings which are characteristic of acute salpingitis from any cause, if existing for some time.

As the acuity of the process subsides proliferation of the surface epithelium becomes evident in many instances. The proliferation may become so marked as to imitate carcinoma closely (Neu, 35).

Kraus (35a), in 60 cases of inflamed tubes, found no proliferation in 38, in 13 there was slight evidence of stratification, in 6 considerable, in 3 the epithelium sent solid blocks or strands into the stroma.

Even in the acute stage strandlike infiltrations in the musculature of the tubes are noted (leucocytes, lymphocytes and plasma cells). The exudates are perivascular and between the muscle bundles. *Abscesses* may develop in the wall (Fig. 240) and later lead to fistulae which become lined with mucosa (see salpingitis isthmica nodosa).

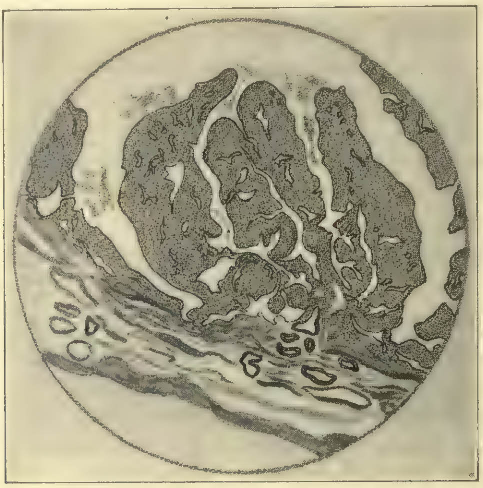

FIG. 239.—EARLY STAGE OF ACUTE SALPINGITIS. So-called catarrhal. (Low power.) The tubal mucosa has become thick and the folds appear fingerlike, because of round-celled infiltration of the stroma. The epithelium is unchanged. The small amount of exudate in the lumen consists mainly of mucus, desquamating epithelium and a few leucocytes. The musculature is unaffected. The blood vessels of the mucosa are dilated.

Peritubal adhesions appear if the infectious contents of the tube soil the neighboring pelvic peritoneum. Such *perisalpingitis* may be the only lesion if the tubes are secondarily involved in the course of peritonitis from any source (especially the right tube from appendicitis), but an endosalpingitis may also be set up (Bland-Sutton, 36). Sometimes a severe puerperal streptococcic peritonitis in which the ascending lymphatic infection has spared the tubes, produces not only a perisalpingitis, but, penetrating the muscular tubal walls, initiates an *interstitial salpingitis* and if the process continues, causes *endosalpingitis* of destructive character (Fig. 240) as the final stage.

The histology may bear evidence as to the mode of infection; in perisalpingeal onset the serosa will show the most pronounced and oldest form of lesions.

FIG. 240.—ACUTE DESTRUCTIVE SALPINGITIS OF PUERPERAL ORIGIN. (Very low power.) The mucosa is deeply infiltrated and partly destroyed. The lumen contains exudate. A peritubal (mesosalpingial) abscess occupies the edematous mesosalpinx.

FIG. 241.—ENDOSALPINGITIS CYSTICA SIVE FOLLICULARIS OF MARTIN. (Low power.) Showing labyrinthine cavities due to adhesion of the folds of mucosa. The tubal wall is thickened.

Chronic salpingitis shows the permanent results of the inflammation. The tubal folds are thickened by connective tissue increase; agglutination of adjacent folds are common and may, on section, appear as intricate labyrinthine cavities (pseudo-follicular, or endosalpingitis cystica sive follicularis of Martin (Fig. 241). In certain cases atrophy of the mucosa supervenes.

FIG. 242.—ACUTE EXACERBATION OF AN OLD SALPINGITIS. Two years' duration. (Low power.) At operation there was found marked adhesion to neighboring organs, the mesosalpinx thick, infiltrated and friable, the end of the tube closed, its lumen containing a small amount of thick, ropy pus. Microscopical; the lumen is small, lined with exudate, the surface epithelium destroyed. A few irregular, poorly staining folds appear amid the exudate. The round-celled infiltration has separated the muscle fibers of the tubal wall, especially in the region of the mesosalpinx.

The tubal wall is regularly thickened by connective tissue increase, the muscular elements showing diminution (interstitial salpingitis).

Perisalpingitic adhesions are usually present. The ostium abdominale may be closed. Intimate fusion with the ovary may exist. Acute exacerbations may superimpose the signs of acute inflammation upon the chronic changes already present (Fig. 242).

Closure of the Tubal Ostium.—As the result of salpingitis and of pelvioperitonitis, closure of the peritoneal ostium may supervene. Tuberculosis of the tube forms the most frequent exception. The mechanism of closure is not always the same.

The simplest mechanism results when the ostium is blocked by peritonitic veils or adhesions (Doran, 37) or by adherence of the ovary or intestine to the opening.

Retraction of the fimbriae of the tube to within the inside of a hydrosalpinx or tubo-ovarian cyst has been explained by the fact that the fimbriae are the direct continuation of the intratubal folds. Inflammation, through swelling and edema, causes functional occlusion at the rigid peritoneal ring situated at the base of the fimbriae. Distention of the temporarily occluded tube retracts the fimbriae into the tubal lumen (Opitz, 38) or the peritoneal surfaces of the ring thicken, the fimbriae are gradually squeezed inward, and the narrowing ring allows of sero-serous adhesion, producing permanent obliteration of the opening (Ries, 39). For literature see Kaufmann (39a, II, p. 981).

Hydrosalpinx results from accumulation of clear fluid in an occluded tube usually the result of a low grade of inflammation. The tubal walls become paper thin, translucent, parchmentlike membranes. Adhesions may be absent. The condition is frequently bilateral.

Often the fimbriae are found within the sac, radiating from the obliterated ostium. The mechanism through which this occurs has been explained in the previous paragraph. On opening the tube, if the hydrosalpinx is of short duration the tubal walls may contract and the resulting specimen closely resemble a normal tube. More often all contractility has been lost, the walls remaining parchment-paperlike with the mucosa pale and thin.

Very rarely a hydrosalpinx results from the absorption of the pus of a pyosalpinx (Bland-Sutton, 40). From torsion, which, because of the lack of adhesions (in 137 cases, 46 showed none, Martin, l. c., 1), is not infrequent (Kadigrabow, 41, Roeder, 42), an hydrosalpinx may be converted into a hematosalpinx (Bell, 43). The right side seems more often affected by torsion than the left (Kadigrabow, l. c. (41), 26: 10). Large hydrosalpinges, from 1 to 1½ liters, are reported (Pinkuss, 44). The contents are most often sterile. Kelly (45) found a calculus in a hydrosalpinx.

Microscopically the walls of a hydrosalpinx show diminution or entire absence of the mucosal folds. Remains of folds may appear as minute, warty excrescences. The epithelial lining may be cuboidal, low and devoid of cilia (Figs. 243 and 257). Signs of inflammation are rarely absent.

The fluid is thin, colorless to yellowish, neutral or faintly alkaline, of low specific gravity and contains albumen. There may be epithelial cells, leucocytes and debris in it.

Hydrops tubae profluens consist in the periodic discharge of clear fluid through the tubo-uterine ostium and into the vagina supposedly from a

hydrosalpinx. A number of cases are recorded (Findley, 46, Martin, 46). No absolute proof of the tubal origin of the fluid has been given. In one supposed case the discharge continued after removal of the hydrosalpinx (Keith, 47). For literature see Llewellyn and Benton (47a).

Tubo-ovarian cysts usually arise from coalescence of a hydrosalpinx with an ovarian cyst (most often follicle cyst, simple cyst or cystic corpus luteum) and subsequent absorption of the intervening septum.

Occasionally the communication is established by means of a cyst interpolated between ovary and hydrosalpinx. Rarely a tubo-ovarian abscess gradually changes into a tubo-ovarian cyst. For mechanism and literature see Preiser (48). Carcinoma in a tubo-ovarian cyst has been described by Orthmann (49), 10 cases). Hydrops ovarii profluens is recorded by Nassauer (50), the ovarian cyst discharging into the uterus by way of the tube.

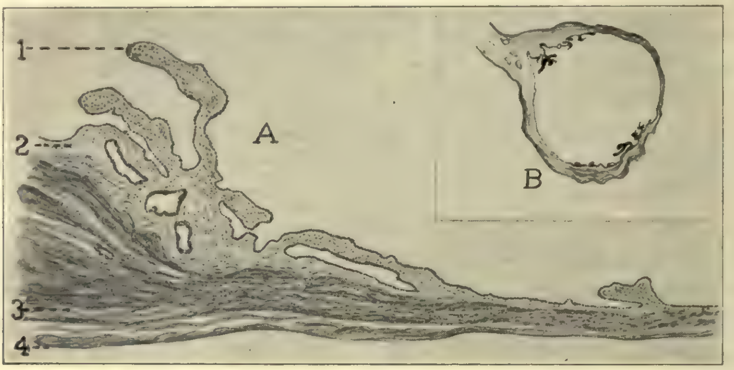

FIG. 243.—TUBAL WALL IN HYDROSALPINX. A. Section of wall. (Medium power.) 1. Folds of mucosa, atrophic and fibrous, are covered by low cuboidal epithelium. 2. The base of the mucosa. Note that it thins out more and more toward the right. 3. Thin muscular wall of the tube. 4. Peritoneal surface. B. (×6.) Cross-section of the tube with a few mucosal folds projecting as small papillae. The tubal wall is thinned out by pressure.

Pyosalpinx.—When during a severe infection of the tube closure of the ostium occurs, the resulting closed cavity soon fills with purulent secretion. The tubal walls almost invariably hypertrophy greatly. Retort-shaped tumors which embrace the ovary in their concave border result. Dense adhesions usually bind the pus tube firmly to the posterior surface of the uterus, to the bottom of Douglas's cul-de-sac and to adjacent loops of intestine.

Not infrequently peritubal abscesses develop. Especially in the acute stages of puerperal infections, pelvic exudates distend the subperitoneal connective tissue and the base of the broad ligaments. Purulent lymphangitis and cellular abscesses are not uncommon. Pelvic peritonitis is the rule.

Latent periods during which absorption of exudation takes place may convert the peritubal adhesions into dense scar tissue.

The pus may be thin, milky, yellow or greenish and, in the later stages, inspissate and then become caseous, chalky or infiltrated with lime. It may have a foul or nauseating odor.

Irregular dilatation or constriction by bands may subdivide the lumen of a pus tube into distinct cavities or sacculations. The closure of the abdominal ostium is usually complete, no trace of the opening remaining externally visible. Closure of the uterine end is commonly functional only. Very rarely, when adhesions are absent *torsion* of a pyosalpinx has occurred (Anspach (51), 12 cases from literature).

A pus tube may remain latent, especially after its contents have become sterile. Exacerbations of the peritubal inflammation at irregular intervals are frequent.

Rupture into the peritoneal cavity, which has been shut off by adhesions, is quite common. The writer operated upon a woman of 48 years who

FIG. 244.—SPONTANEOUSLY RUPTURED PUS TUBE WITH CONSEQUENT DIFFUSE PERITONITIS. (×1/1.) Case of Dr. Walter M. Brickner. 1. Point of rupture showing infiltrated mucosa. 2. Accessory tube with open end.

showed acute peritoneal symptoms. A right necrotic and ruptured pus tube was found. The pus was, however, completely walled off by adhesions. Recovery.

Rupture into the free cavity with consequent diffuse peritonitis is rare (spontaneous, post coitus, in labor, trauma, etc.) (Bonney, Brickner, 52) (Fig. 244). Rupture into the rectum (Roux, 53), small intestine and bladder (Auvray, Heinsius, 54) are on record. Gradl (54a), after rupture of a double pyosalpinx into the rectum, noted pregnancy four months later. According to Gellhorn (55), Morris and also Bonifield performed salpingostomy on cases of pus tubes with subsequent pregnancy and labor. Enormous pus tubes have been reported (19¾ pounds, Williams and Hallock, 56).

Bacteriology of *pus tubes* has shown that in approximately half the

cases, the pus is sterile. Gebhard (l. c. 196, p. 444) found 226 of 409 cases sterile; Wertheim (57), 122 of 206.

	Gebhard	Wertheim	Kelly
Gonococcus	92	56	7
Staphylococcus	53	11	1
Streptococcus		6	
Pneumococcus	10	1	
Bact. Coli	7		
Undetermined	15		
Sterile	226	122	30

The histology of pyosalpinx depends upon the acuity of the process and the stage observed. Loss of epithelium usually occurs late unless the

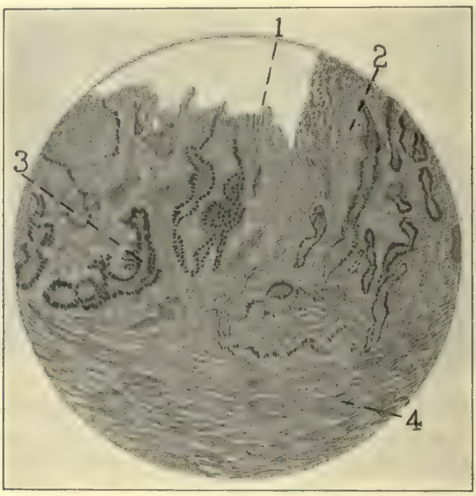

FIG. 245.—PYOSALPINX SHOWING AN ACUTE EXACERBATION. (Medium power.) The lumen was filled with ropy pus, the tubal wall much thickened and infiltrated (only ⅓ of its thickness appears at the lower margin.) The mucous membrane is much damaged. 1. Lumen. 2. Round-celled and leucocytic infiltration filling all interstices between tubal folds. 3. Poorly staining and much damaged fold of mucosa. 4. Infiltrated muscular wall.

infection is virulent. Oftentimes, although the folds are thickened, infiltrated and bathed in pus, the lining epithelium is partially preserved (Fig. 245). As the tube distends the folds flatten out and the mucosa atrophies (Fig. 246). More severe inflammations and older tubes show a pyogenic membrane, streaky, diffuse infiltrations in the musculature and inflammation of the mesosalpinx (Fig. 240). Occasionally necrosis of the tubal wall takes place, more often in localized areas, producing erosion and thinning. Figure 240 shows such a case with an abscess in the mesosalpinx.

Pick (58) has shown that what macroscopically appears as yellowish, purulent material in the wall of old pyosalpinges may, in some instances, really be xanthoma cells, due to disturbance in the cholesterin content or absorption (Anitschkow, 59).

The treatment of tubal inflammations has undergone a radical change. At the beginning of the operative era early and radical interference was the rule, to-day operation is regularly postponed until the acute stage has passed. The reason for this change is twofold. Firstly, if early operation is performed many cases which would return to normal, or become latent, are operated upon. Secondly, the virulence of the infection diminishes with time, self-sterilization of the focus, increased resistance of the peritoneum resulting. The operative morbidity and mortality is thus greatly diminished.

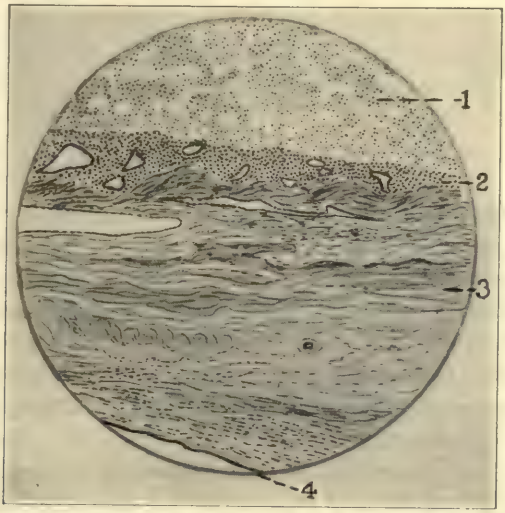

FIG. 246.—PYOSALPINX IN THE CHRONIC STAGE. (Medium power.) The mucosa has become atrophic and fibrous. No trace of projecting folds remain. Residua of folds appear as pockets or glandlike cysts. 1. Pus in the lumen. 2. Mucosa with pockets lined with epithelium. 3. Tubal wall now largely fibrous. 4. Serosa of tube.

Operations performed in the acute stage are also rendered more difficult by edema, induration and friability of the mesosalpinx. If done early, usually complete hysterectomy and subperitoneal vaginal drainage must be performed to avoid persistent exudates.

TUBERCULOSIS OF THE FALLOPIAN TUBES

The tubes are the organs most frequently affected in genital tuberculosis.

According to White (60) the order of frequency is: in tubes 85 per cent; uterus, 53 per cent; cervix, 15 per cent; vagina, 2.5 per cent.

Williams (61) in 8 per cent of all diseased adnexa found tuberculosis, and of these, 75 per cent could only be recognized as tubercular by aid of

the microscope. Pankow (l. c. 20) found 22 per cent of 400 tubal cases tuberculous, Jung (61a) found 24.6 per cent in Martin's material affected.

Fromme and Heynemann (61b), in 884 cases of pyosalpinx from various sources, found 48 tubercular cases, or 5.5 per cent. Here the percentage error of not examining all cases microscopically must be taken into account. In a collection of 17,470 autopsies (p. 164) they found genital tuberculosis in 142, some 0.81 per cent. Doubtless here too many occult cases were overlooked. Merletti (60), in 1360 autopsies on tuberculous cadavers, found 172 tuberculous adnexa, or 12.6 per cent. Schlimpert (61c), in 3514 autopsies of women and girls with tuberculosis, found 3.4 per cent affected with genital lesions.

Vagina alone tuberculous	7	9.6%	Uterus tuberculous......	41	56.2%
Uterus " "	11	15.1%	One tube tuberculous...	9	12.3%
Tubes " "	21	28.8%	Both tubes " ...	42	57.5%
Ovaries " "	2	2.7%	One ovary " ...	3	4.1%
			Both ovaries " ...	7	9.6%
			Parametria " ...	4	5.5%

Mode of Infection.—Goodall (62) considers 99 per cent of genital tuberculosis secondary. Many pathologists believe primary genital tuberculosis does not exist.

Fromme and Heynemann (l. c., 61a) are willing to accept a small number of cases as instances of primary tuberculosis. They accept the 10 cases presented by Veit (63) in his Referat at the International Gynecological Congress at Rome in 1902. To these they add three more (Hammer, Marcheses, Simmonds).

The mode of infection may be (*a*) ascending through the vagina (examinations, masturbation, operation, coitus (Jani, 64), etc., (*b*) entrance at some distant site (as mucosa of respiratory or intestinal tract) without producing a local lesion, (*c*) entrance through a small wound in the genital tract (paravaginal or metritic).

Primary genital tuberculosis may be regarded as a curiosity. Practically all cases have primary foci elsewhere, though in more than half of the cases the foci are not discoverable by clinical means.

The primary focus is most often pulmonary or from bronchial glands. Infection is metastatic by the blood stream. Infection by continuity occurs from the peritoneum, the intestine, mesenteric glands or from the genito-urinary system. Infection conceivably can come from the lower genital tract, though this mode must be uncommon.

Kaufman (l. c. 39a, II, p. 983) has shown how well hidden the primary focus may be (bronchial lymph-node, scars, etc., four cases). Keller (65) reports two cases of tubal tuberculosis which died shortly after operation, in whom careful autopsy failed to reveal a primary focus. On the other hand Horizontow (66) in collected statistics found that in genital tuber-

culosis the lungs were involved in 89.5 per cent, the peritoneum in 64.2 per cent, the intestine in 56.4 per cent and the urinary tract in 42.4 per cent.

Merletti (66a) regards hypoplastic genitals as a locus minoris resistentiae for tuberculosis. In 80 cases, 24 were tuberculous.

The age of occurrence is commonest between the sixteenth and twenty-fifth year. White (l. c. 60) found the age distribution in 253 cases as follows:

Below 15 years	15	cases
16 to 25 "	119	"
26 to 35 "	77	"
36 to 45 "	38	"
46 "	14	"

Children of one year or more can be affected (Hohlfeld, Graefe, 67). Williams (l. c. 61) mentions a case at 10 months and one at 83 years.

Macroscopic Appearance.—In 75 per cent of instances, according to Williams, l. c. 61), tuberculous diseased adnexa cannot be distinguished from those due to other infecting organisms.

Most characteristic is the fact that in nearly half the cases the ostium abdominale remains open (Fig. 247), and cheesy material may project from it. This accounts for the frequency of peritubal abscesses which may encapsulate and in rare instances retain communication with the open tube (Knauer, 67a). In 60 per cent of Kaufmann's (l. c. 39a, II, p. 982) autopsy material, tuberculous peritonitis co-existed, in Hartmann's (67b) operative cases 26 of 28 had peritoneal involvement, yet this sign may be of little value, as in 109 cases of this disease, Blau (68) found the tubes showing macroscopic evidence of involvement in only 20.

In more advanced cases the thickened, retort- or rosary-like tubes are doughy in consistence. Pyosalpinges of large size may form (Werth, 69), two liters).

Their gray-white, firm walls lend them considerable resemblance to thick-walled ovarian cysts. Rupture into the bladder (Heinsius, 70), fistula formation with the rectum (Kaufmann, l. c. 39a, II, p. 982), openings into the free peritoneal cavity (Fabricius, 71), fistulae through the abdominal wall, torsion (Forssner, 72), may occur.

In the gross specimen the yellowish-gray, sago-like tubercles on the surface of the tube and mesosalpinx (Fig. 247) will, if present, help in the recognition of the tuberculous nature of the trouble. On opening the tube in early cases similar tubercles are found in the mucosa. Later cases show caseating masses which fill the lumen, and ulcers on the mucosa with complete destruction of this layer and substitution by caseous material. The tubal wall usually is infiltrated, hard and greatly thickened. Interstitial cheesy masses, or hernialike protrusions toward the serosa may be noted (Fig. 247). A chronic fibrotic (healing) stage, marked by much connective

tissue is described by Williams (l. c. 61), Fränkl (73) (Fig. 250). All these varieties are partly accidental variations, partly different stages of the tuberculous invasion. The isthmic part of the tube is often unaffected or shows so-called salpingitis nodosa.

The histology in most ways is characteristic of tuberculosis everywhere in the body—epithelioid tubercles, necrosis and caseation. The amount of ulceration and loss of substance depends upon the acuteness and duration of the process. The thickening from fibrosis is most evident in healing chronic cases. Tubercle bacilli are readily found in acute cases, but become harder to demonstrate as caseation increases.

Fig. 248 shows an acute miliary endosalpingitic type with some thickening of the surface epithelium.

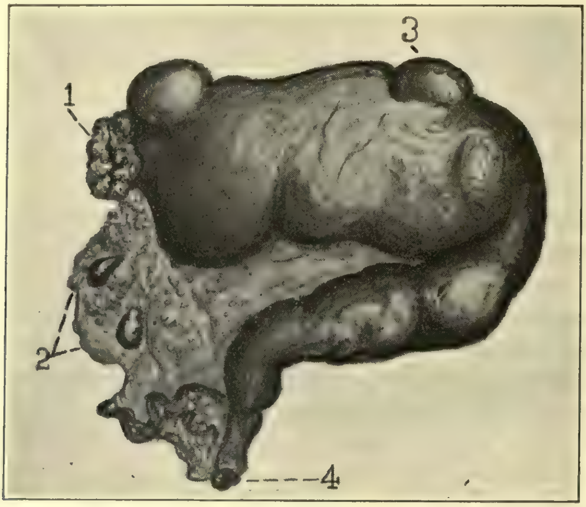

FIG. 247.—TUBERCULAR PYOSALPINX. (×1/1.) The retort-shaped pus tube shows open abdominal ostium (1). Spreading from here along the meso-salpinx are numerous miliary tubercles; also note two small inflammatory cysts on the meso-salpinx (2). Two nodular hernial projections along the upper surface of the tube (3). The uterine end of the tube appears normal (4).

Fig. 249 shows a more advanced and subacute case in which the mucosa has been destroyed and the muscular wall riddled with epithelioid tubercles. A strong fibrous overgrowth has walled off the process toward the serosa.

Fig. 250 shows a chronic fibrous stage in which the tube on cross section macroscopically looked like a thick fibrous cord. The lumen is small, the mucosa replaced by firm caseated tubercles. A thick, fibrous, interstitial layer has formed.

v. Franqué (74) and others have described changes in the epithelium covering the folds. The layers become multiple, small papillae may develop. The cells appear polymorphous, irregular in size, the protoplasm is cloudy, the nuclei vary in size and shape. The atypical development has been

regarded as precancerous (Barbour and Watson, 75) and cancer has arisen in such tubes (p. 352).

Fig. 248.—Acute miliary type of endosalpingitis. (Medium power.) Shows folds of the mucosa containing three typical epitheloid tubercles and giant cells. The surface epithelium is thickened. A few leucocytes and plasma cells occur between the folds in the lumen of the tube.

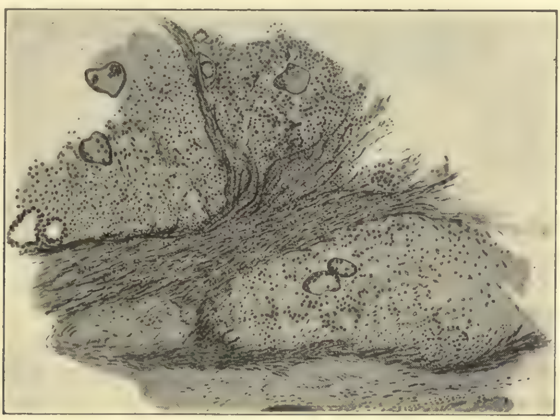

Fig. 249.—Subacute diffuse tuberculosis of the fallopian tube. (Medium power.) Above are shown numerous epitheloid areas with giant cells, largely replacing the mucous membrane. In the middle are muscle fibers showing round-celled infiltration. Below and to the right large tubercles substitute the destroyed muscle. At the bottom are remnants of the muscle wall.

Papillary elevations in tuberculous tubes, grossly resembling tumors, are reported by Gaitami (76) and Montanelli (77).

Stumpf (77a), in a tuberculous tube, found numerous giant cells in

almost every one of which was contained a calcium concretion at that portion of the periphery most distant from the nuclei.

The final outcome of tuberculosis of the tubes is various. Healing doubtless can take place or fibrosis encapsulates the focus. Usually, however, the uterus and more rarely, the ovaries (Cohn, 78), play a rôle in the further course. Peritoneal infection is common (*vide ante*) and reinfection of the peritoneum from apparently normal tubes is claimed by Mayo (79). According to Kraus (80), after abortion or labor the tubes may activate a general miliary tuberculosis.

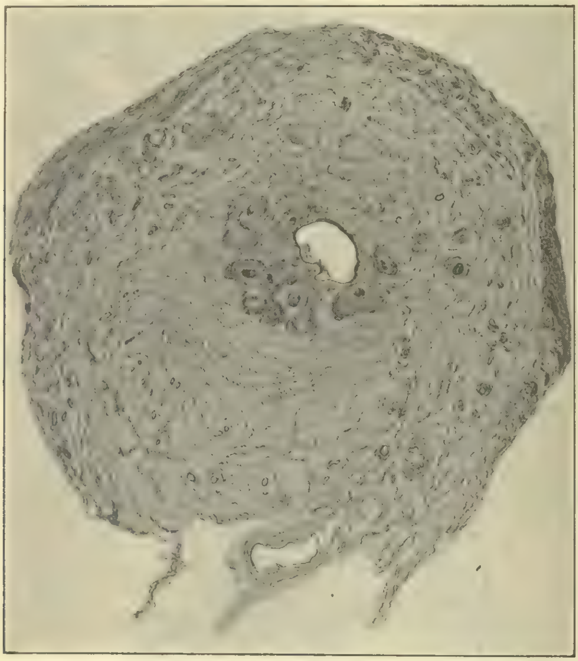

FIG. 250.—FIBROUS STAGE OF TUBERCULOSIS OF THE TUBE. (Healing.) (Very low power.) The small lumen is surrounded by numerous caseating areas, among which tubercles with giant cells can still be distinguished. Enormous hyperplasia of the outer coats has resulted from the mainly fibrous replacement of the musculature.

The prognosis is not bad. Krönig (81) emphasizes that at the autopsy table genital tuberculosis almost never is found to have been either a cause or even an accessory cause of death.

Veit (82) in 1902 advised extreme conservatism in operation. From what has been said it will be plain that a majority of cases are operated upon without the diagnosis of tuberculous salpingitis having been made.

In cases in which overt tuberculosis elsewhere exists, non-interference should be the rule. Exception should be made when at operation for the ascitic type of peritoneal tuberculosis, tuberculous tubes are found. Under these conditions they should be removed. Where the probability of tubal

tuberculosis exists (recognizable foci elsewhere—pulmonary, intestinal, urinary) treatment along hygienic lines is indicated. Patel and Olivier (83) reported on 116 cases operated upon for genital tuberculosis:

9 died after operation.
8 died later of tuberculous peritonitis.
19 were alive but could not be examined.
80 were alive for periods of a few months to eleven years, of these 72 were in good health.

FIG. 251.—SALPINGITIS NODOSA. (Adenomyoma of the tubal angle.) (Very low power.) Transverse section through a nodule near the uterine end (the ampullar portion being typically tubercular). Thickened tube, lumen semilunar on section, above it numerous cystic cavities in cytogenic stroma. Below note the lumina in the mesosalpinx.

The post operative course is marked by the great number of intestinal fistulae (4 in 28 cases, Geist, 84) and breaking down of abdominal wounds (5 in 28).

Pregnancy has been noted in a case of early double tuberculous salpingitis (Schröder and Rau, 84a).

Salpingitis Nodosa (*isthmica or interstitialis*).—Salpingitis nodosa is the residuum of an inflammation. The condition has already been referred to in connection with adenomyoma (p. 213).

Chiari (85) in 760 autopsies of females found small, myoma-like enlargements at the tubal angle in 7 cases. He regarded them as of inflammatory origin. Schauta (86) gave the condition its name. v. Recklinghausen (87) confused the issue by ascribing the origin to wolffian rests.

Hoehne (88) and Maresch (89), by means of serial sections, showed continuity with the tubal lumen and an origin from wall abscesses which perforated into the tube, the fistulous tract being subsequently lined with epithelium.

Jayle and Cohn (90) subdivide the growths into gonorrheic, tuberculous, simple and angiomatous. Wallert (91) and also Rabinowitz-Robinson

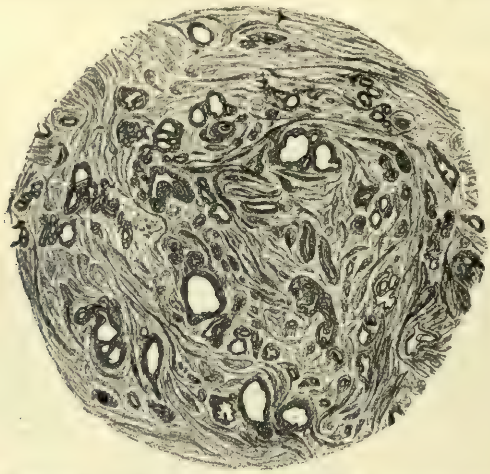

FIG. 252.—SALPINGITIS NODOSA. (Low power.) Conforms to the adenomyoma type with glandlike spaces surrounded by cytogenic tissue, with an outer mantle of muscle.

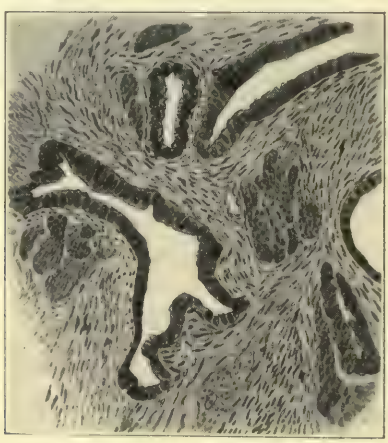

FIG. 253.—SALPINGITIS NODOSA. (High power.) Glandlike spaces lined with cylindrical epithelium and surrounded by unstriped muscle without interposition of cytogenic stroma.

(92) emphasize the frequency of antecedent tuberculosis (Fig. 251). Santi (93) found marked decidual reaction of the cytogenic tissue in an adenomyoma in a case of interstitial pregnancy. A psammocarcinoma has been reported as metastasizing in a focus of salpingitis nodosa (Boxer, 93a)

and Iwanow (93b) describes papilliferous elevations in what evidently is an area of salpingitis nodosa. For other details see Adenomyoma, p. 210.

Fig. 252 shows an adenomyoma of the interstitial part of the tube in which undilated and dilated canals surrounded by cytogenic tissue and muscle are found. Fig. 253 gives a high-power picture of another adenomyoma in which the canals are surrounded by muscle without the interposition of a cytogenic stroma.

SYPHILIS OF THE TUBES

Considerable literature has been published concerning this condition, but none of the recorded cases stand the test of our modern knowledge.

Gellhorn and Ehrenfest (94) in their monographic report to the American Gynecological Society summarize as follows: "It seems possible that the tubes may be the seat of luetic lesions, but the pathological and clinical material on record is yet too incomplete to permit of positive assertions. Spirochetes have never been found in the tubes of syphilitic women."

These authors carefully reviewed the cases regularly quoted and decided that the evidence is insufficient.

Hoffmann's case (95) in which the entire genital tract was involved in gummatous changes and which showed gumma of the right tube, must be considered exceptional. In a somewhat similar case of Gellhorn's (96) the tubes were not involved.

The cases regularly referred to are:

Bouchard and Lepine (97), tubal gummata.

Doenhoff (98), newborn syphilitic child. Tubes tortuous, stiffwalled, infiltration of walls and mucosa.

Ballantine and Williams (99), tubes of a luetic fetus.

Wassilieff (100), by operation, obtained tubes in four cases of luetic women. He finds the tubes thickened and their color indigo blue in the early stage. The late stage is characterized by pale, thin, sclerotic tubes. Microscopically, sclerosis and periarteritis are found.

For a conservative and yet charitable review of the few and almost fanciful observations recorded, the reader is referred to Gellhorn and Ehrenfest's article (l. c. 94). Ozenne (101) records without critique, and apparently accepts the literature usually quoted.

ACTINOMYCOSIS OF THE TUBES

The tubes are only secondarily involved when abdominal actinomycosis invades the genital tract. Of 20 cases of adnexal actinomycosis collected by Robinson (102), 10, or 50 per cent, showed involvement of the tube.

The tubes are involved in the general mass of dense, indurated adhesions, granulation tissue and collections of pus which characterize the infec-

tion. Their lumen may be lined by granulation tissue which replaces the mucosa. Conglomerate tumors consisting of ovary and tube may be found (l. c. 102). The destruction may be so extensive as to remove all trace of the adnexa, as in Bondy's case (103). To assure the diagnosis mycelia must be demonstrated.

The prognosis is that of advanced abdominal actinomycosis, i.e., bad. Removal of the focus, if possible, is indicated.

For literature see Hamm and Keller (103a), Robinson (l. c. 102), and Fromme and Heynemann (l. c. 61b, Veit, V, p. 180).

NEOPLASMS OF THE FALLOPIAN TUBES

New growths of all kinds are of uncommon occurrence in the tubes and except for malignant tumors, are unimportant clinically.

It has been the custom wrongfully to include among tubal growths a number of inflammatory conditions. Among these are:

Serosal cysts which begin as encapsulations of fluid in the course of a pelvic peritonitis and later are found lined with cuboidal epithelium (or endothelium) enclosed by a fibrous wall (see p. 214) (Fig. 247).

Herniae of the tube, due to weakening of the tubal wall. Through the weak spot a pouch of mucosa is squeezed. They are seen especially in tubercular pyosalpinx (Fig. 247) and are called "paratubal" cysts by Lockyer (Eden and Lockyer, l. c. 60, II, p. 715).

Adenomyomata or *adenomyositis* of the tube, especially so-called "fibroids" which concentrically surround the tubal lumen. All of these are residua of inflammation and should be classified as salpingitis nodosa (see p. 345).

Calcifications in the tube, tubal stones (Orth, 104) and "cysts" filled with cheesy detritus often in combination with calcification. Such findings usually are residua of an old tuberculosis. Calcification of the fimbriae also occurs (Kermauner, Strassmann, 105).

Ossification has been observed seven times. In each case it was due to some preceding inflammation. The process consists of necrosis, calcification, and ossification as the final stage (Pozzi and Bender, Strong, Lehmacher, 106). The last named author found bone and marrow. Such cases should not be described as "osteomata."

Cysts.—With the exception of three cases, Stolz (107) 12 cm. and Boldt (108) 3 inches in diameter, Oginz (112) coconut size, such cysts are unimportant accidental findings.

Lymphangiectatic cysts or dilatations are seen especially in connection with myomatous uteri, and most often where large varicose broad ligament veins abound. The cysts may be small and numerous, bulging out the serosa over the tube and meso-salpinx, or elongated dilatations like the beads of a rosary along the lymph vessels. Their wall is thin, translucent and lined

with flat endothelium. The contents are clear, colorless or yellowish and of mucoid consistence.

The hydatid of morgagni is a cystically changed fimbria. Its presence may be regarded as physiological. The small, translucent, thin-walled cyst is lined by low cuboidal cells. Klob (109) reported its enlargement to 7.5 cm. in length.

Andrews, and also Waters (109a), report torsion of the hydatid which was 2 × ¾ in. and produced symptoms resembling appendicitis.

Although this little body is so unimportant, it has given rise to much controversy. Kobelt (109b) considers it an elongated tubal fimbria, Waldeyer (109c) a fluid sac secondarily formed at the infundibulum, Nagel (109d) the blind upper end of the wolffian duct, Köllicker (109e) a lymphangiectatic dilatation, Handley (109f) of pronephric origin. For literature see Kaufmann (l. c. 39a, pp. 977 and 955) and Peters (109g).

Hydrosalpinx of an accessory tube forms small pedunculated cysts attached to the tube anywhere in its course (Kossmann, 110). Bell (111) demonstrated a large specimen.

Thaler (111a) showed a left tube with two accessory cystic tubes and a right tube with a large cyst. In all three accessory appendages, in spite of their cystic change, the fimbriae could be plainly discerned.

Torsion of the tube by a large cyst (coconut size) of the tube is reported by Oginz (l. c. 112). The cyst arose subserously and several fimbriae were attached to it.

Fibroma and Fibromyoma of the Tube.—As a rule only small, single tumors either sessile or pedunculated originate in the tubal wall. Auvray (113), who has collected 32 cases from the literature, described one tumor weighing more than 2 kg. In 934 cases of uterine fibroids Kelly and Cullen (113a) found only one tubal myoma.

Rudolph's (115) case was a pure fibroma. It was the size of a pigeon's egg and intraligamentous. Herde (115) reports a pure fibroma of the abdominal end of the right tube which caused a torsion of the tube.

Auvray's case (l. c. 113) arose from a blind malformed tube which was closed and formed a hydrosalpinx. This author states that only one case was bilateral. In three cases the tumor arose from the fimbria ovarica. The tumors may be subperitoneal, interstitial or submucous. They show the same constitution and may undergo the same changes as fibromyomata do elsewhere (hyaline changes, calcification, necrosis, etc.). In two instances ectopic pregnancy coexisted.

Adenomyomata, and nodules due to salpingitis nodosa, are often erroneously classified with fibromyomata.

Lipoma.—Lipoma is even more uncommon than fibroids. Sänger and Barth (l. c. (1) Martin's Handbuch) mention the occurrence of small accumulations of fat in the outer third of the meso-salpinx of fat women.

A small intraligamentary lipoma with tubal mucosa running through it

is described by Parona (116) and a small pedunculated lipoma hanging from the fimbria ovarica by Doran (117). The former may have been a broad ligament lipoma infiltrating the tubal wall.

Osteoma.—This has been described under ossification. Apparently the presence of bone is due to inflammatory metaplasia (see p. 348).

Enchondroma.—Like osteoma, this, probably, is due to metaplasia in most cases. The cases of Thiébault (118) and Jacobs (119) appear to belong to this class—calcification and cartilage cells.

v. Franqué's and Outerbridge's cases belong among the mixed tumors—see below.

Lymphangioma.—The five cases on record have been described in some detail. The tumor is found as a pea- to cherry-sized nodule which lies between the muscle fibers of the tubal wall. The tumors are gray-white with baconlike sheen. In all cases the uterus contained myomata.

The histology is characteristic. A dense conglomeration of lymph-capillaries with marked endothelial proliferation is found. The endothelium is stratified in many spots. In Leighton's case (120) the tumor was surrounded by lymphoid tissue. Kermauner (121) considered the growth as potentially malignant. The other cases were reported by Dienst, Franz (122).

Endothelioma.—Kvorostansky (121a) describes a marked proliferation of the vascular endothelium as an endothelioma. The endothelium filled the lumen of the lymph vessels.

Kermauner and Lameris (121b) report a small tubal metastasis from a uterine endothelioma.

Mixed Tumors, Dermoids and Teratomata.—Mixed tumors are uncommon. Outerbridge's case (123) in which a polypoid growth was found lying free in the tube, uterineward from a tubal pregnancy, is the only non-malignant type of its class. The growth contained cartilage, fibrous and fatty tissue.

Perhaps the polypoid fibro-myxoma cysticum of the tubal fimbriae described by Sänger and Barth (Martin, l. c. (1), p. 295) belongs among the non-malignant mixed tumors. The growth consisted of numerous cystic pedunculated vesicles depending like a bunch of grapes by three pedicles from the tubal fimbriae. Their surface was covered with ciliated epithelium, but the stroma, which was myxomatous, contained no epithelium except where glandlike projections from the surface grew inward.

Of malignant mixed tumors several are on record. The best representative is v. Franqué's case (124) which he classified as a carcino-sarcomatous endothelioma containing hyaline cartilage. Sänger (125) and Schäfer (126) and Spencer's (127) case IV are classifiable as carcinosarcomata, Amann's case (128) as a chondrosarco-carcinoma.

Such tumors produce ascites, peritoneal implantations and glandular metastases (inguinal, Sänger, l. c. 125).

Dermoids and Teratomata.—About one dozen cases are recorded. The tubal wall may form the outer envelope, the dermoid "anlage" being a small pedunculated growth as in Orthmann's case (129), or the dermoid cyst may grow into the tubal lumen and then secondarily perforate as in Pozzi's. Grossly the specimens appear as simple, non-adherent thick-walled sactosalpinges containing either fluid or thick sebaceous contents. Somewhere on the wall or free in the cavity is a hairy, finger- or cocoonlike body.

The ectoderm is represented by hair, sebaceous and sweat glands; glia and central nervous system and a tooth in Orthmann's case. The mesoderm is represented by fat tissue, unstriped muscle and cartilage, the entoderm by ciliated epithelium and mucous glands.

Stark's case (131) was bilateral. Noto's case (132) had calcareous incrustations and bony scales, the wall being 0.5 to 1 cm. thick. In Lockyer's (133) case the tubal walls were paper thin. In Pozzi's case (l. c. 106) a tubal pregnancy existed on the other side, in Noto's (132) double cystic ovaries, in Jacobs' (134) multiple myomata. Ritchie's (135) report is doubtful because the mass was multilocular, the walls were lined with serosa-like membrane and no microscopical examination was practiced. Other cases are those of Schouwman, Potherat, Prochownik, Roberts, Sneguiereff, Müglich and Ostreil (136).

PRIMARY CARCINOMA OF THE TUBES

Primary involvement of the tubes by cancer was first recognized by Orthmann (137). In 1917 Lockyer (l. c. 60, II, p. 745) accepted 137 cases. Frankl (137a, p. 179) speaks of 150 (probably accepting Lipschitz's statement of 144 cases in 1914—l. c. 146). Since then at least five additional cases have been added (138).

So-called *polypi* of the tube such as Wyder (138a) described are probably either thickened tubal folds or placental polypi, due to tubal pregnancy.

Lahm (138b) describes a polyp arising from a "paratubal tract" (salpingitis nodosa) projecting into the tubal lumen. There was an intra-uterine pregnancy. Only the polyp and the submucosa of the salpingitis nodosa glands showed decidual reaction.

The so-called *benign papilloma* of which Doran (139) in 1879 described the first case, and of which Lockyer (l. c. 60, II, p. 745) up to 1910 had collected 19 cases (although his own count makes them 16) appears to bear the same relation to carcinoma of the tube as "adenoma" of the cervix bears to cervical cancer (see p. 289). The epithelium has been described as always in a single layer. Clinically these growths are supposed to be non-malignant —Doran's case (Case I) was well after 23 years, Bland-Sutton's Case II, after 15 years, Doleris Case I, after 27 years.

The frequency of occurrence of cancer according to Vest (140) in 19,000 gynecological cases was 4, according to Zangemeister (141) in 374 laparotomies for tubal trouble 5, or 1.33 per cent.

The *age* occurrence is most frequent around the climacterium. Of Theilhaber and Edelberg's (142) 61 cases, 35, or 57.4 per cent, were between 41 and 51, of Vest's cases (l. c. 140) 53 per cent, the average age of 127 being 48.3 years. Norris's case (143) was 27 years of age.

Etiology.—Orthmann (144) found signs of antecedent inflammation in 51.7 per cent of 84 cases. LeCount (145) likewise favors this view. v. Franqué, Lady Barret and Lipschitz (146) described chronic tuberculosis co-existing in their cases. As in other organs, wolffian remains (Doran, l. c. 149) and malformation (accessory tube, Friedenheim, 147) have been mentioned. It appears to the writer that the relation between cancer and chronic irritation is more evident in the tube than in any other organ of the genital tract.

Macroscopic Appearance.—Most often cancer produces a sausage-shaped enlargement of the middle and outer third of the tube. The surface may be smooth or lobular, only in advanced cases was the outer surface finely nodular (Peham (148), 6 of 63 cases). In larger growths the wall is often greatly thinned. Adhesions to neighboring organs are frequent. About one-third of the cases are bilateral (Doran, 36 per cent (149), Kehrer (150), 32.8 per cent). The size may reach that of a child's head (Stolz, 151). In Cullen's case (152) the tumor was $14 \times 12 \times 10$ cm.

On incising the tube, small localized papillary or villous masses growing from the mucosa are found in early cases. At a later stage the distended tube, except the inner third, may be filled with papillary growths. In spots necrosis may have taken place. More rarely the entire growth or parts of it may be nodular, white, soft and "encephaloid." This latter type of case shows earlier tendency to penetrative (endophytic) growth. The surface of the mucous membrane always appears to be the starting point.

According to Orthmann (l. c. 144) the ostium abdominale is closed in 51 per cent, according to Fromme and Heynemann (l. c. 61b), in 50 per cent. Occasionally cancerous masses protrude from the open abdominal ostium (Kehrer, l. c. 150) causing early peritoneal involvement.

Sactosalpinx was present in 26, tubo-ovarian cyst in 10, the ostium closed in 7 of 84 cases collected by Orthmann (l. c. 144).

Rupture during examination occurred in Orthmann's case (l. c. 144), spontaneous rupture with subsequent peritonitis in Kiwish's (153), growth through the tubal wall in Fischel's (154).

Ascites is often present (Kehrer, 150). In Doran's patient with papilloma (l. c. 139) a pleuritic exudate was also found. The tube regularly contains sero-sanguinous fluid in which detritus, swollen cancer cells, leucocytes and red blood cells are found.

Metastases, according to Lipschitz (l. c. 146), occur in 28 per cent (?). The lymph glands were involved 7 times in 43 cases (Stolz, 155). Both

the pelvic and inguinal glands may be affected (v. Rosthorn, 156). The ovary is often involved (Cullen (157), v. Franqué (l. c. 146), Kehrer, l. c. 150). Metastases in the liver (Westermark and Quesnel, 158) and bladder (Kehrer, 150) have been noted. The peritoneum shows implantations, which occur also in the omentum, rectum, diaphragm (Fónyo (159), Lipschitz, l. c. 146), and small intestine (Hörrmann, 160). The parametria may be infiltrated as in cervical cancer.

Hofbauer (160a) reported a bilateral cylindrical-cell cancer of the tubes and squamous-celled cancer of the cervix, Kundrat (l. c. 164) tubal cancer with metastases in the corpus and cervix uteri.

Recurrences are usually peritoneal and local. Osterloh (161) first discovered that his case was one of carcinoma when one year after salpingectomy for supposed pyosalpinx, an implant appeared in the abdominal wound. Hartmann (l. c. 138) reports a wound implant, together with breast metastases occurring two years after operation—reoperation and well being for at least one year.

Prognosis.—The outlook is unfavorable. According to Doran (l. c. 149), 25 per cent die of recurrences within one year. Kehrer (l. c. 150) in 80 cases found only 5 cured, or 6.2 per cent. The diagnosis is not made and operation performed too late. Often at operation the apparent sactosalpinx (pyo- or hydro-salpinx) is not opened. See Osterloh (l. c. 161). A radical hysterectomy is indicated.

Cures of long duration are on record—Wiesinger (162) Case I, 13 years; Case II, three years; also Fónyo (l. c. 159) Case II, three years.

Histology.—Apparently papillary adenocarcinoma predominates, as Lockyer (l. c. 60, p. 754) finds only 19 "benign" papillomata, i.e., "adenoma malignum" with single layer of epithelium, to use the nomenclature employed in uterine cancer, to 137 other cases. Vest (l. c. 140) of 29 cases, classed four as adenocarcinoma, the rest as papillary.

The papillary type must be considered largely due to mechanical conditions resulting from the freedom from pressure in the tubal lumen. These same growths when infiltrating the tubal wall show alveolar character. Kehrer (l. c. 150) very properly considers the papillary form the early, the alveolar the late stage. The benign papilloma should be regarded as a still earlier stage.

Squamous carcinoma of the tubes was found by Orthmann (l. c. 144). Hyaline pearls in the center of alveoli by Fónyo (l. c. 159). v. Rosthorn's (l. c. 156) and Friedenheim's case (l. c. 147), in spite of careful search, showed no papillary portions. Boxer reported a psammo-carcinoma (l. c. 93a).

The papillary cancer shows a multilayered polymorphous epithelium upon a fibrous framework. The papillae may be so densely crowded as to appear a solid mass of cells with sparse septa. Indications of glandular formations occur.

The adenocarcinomatous type resembles that found in the uterus and shows transitions to more solid types (carcinoma simplex, see Fig. 254).

FIG. 254.—PAPILLARY CARCINOMA OF THE FALLOPIAN TUBE. (Medium power.) The mucosa has been destroyed and substituted by the growth. The neoplasm lines the lumen (1), and invades the musculature. Cancer alveoli varying in type from solid to adenomatous, appear in a fibrous stroma (2). The tubal wall (3) is thickened and shows signs of antecedent inflammation.

SECONDARY TUBAL CANCER

Secondary cancer occurs most frequently in ovarian cancer, next in frequency from corporeal, cervical and gastric carcinoma (after the ovary has become the seat of metastases). In general abdominal carcinosis, the peritoneal surface of the tube may be studded with miliary nodules, or contain large nodes extending down through the musculature into the serosa; or more rarely the tubes are open and distended like full cornucopias overflowing with cancerous material (Kaufmann, l. c. 39a, II, p. 984).

The involvement in ovarian cancer is most frequent and early. As Lockyer (163) has shown, normal appearing tubes may contain microscopic lymphatic metastases in the tubal wall and folds.

In corporeal cancer the tube is involved not too infrequently (Chapter VIII, Cullen (l. c. 66, p. 157), Schottländer and Kermauner (l. c. 190a, p. 618), Kundrat, l. c. 222). Extension by continuity, along the lymph channels or even on the mucous surface are on record (see Chapter VIII, p. 301).

In cervical cancer tubal involvement is rare in operable conditions (Kundrat, 164), but more frequent at autopsy (Taussig, 165, lit.).

In cancer of tubo-ovarian cysts (Orthmann (l. c. 144), Lipschitz, l. c. 146) it may be difficult or impossible to determine whether tube or ovary is the primary focus, as papillary tumors of the ovary resemble tubal cancer in morphology.

Krukenberg cancers of the stomach first involve the ovary and then attack the tubes (Glendinning, 166).

The histology of secondary cancer conforms to that of the primary focus.

SARCOMA OF THE FALLOPIAN TUBES

Sarcoma is a very rare disease. Only ten cases will bear scrutiny. Four others which are less well authenticated are reported.

The patients were from 27 years (Jacobs' Case II) to 61 years (Scheffzek) of age. In six the tumors were unilateral, in four bilateral. The tubes form sausage-shaped tumors as in pyosalpinx and cancer. Ascites was present in one case. Glandular involvement and abdominal metastases were found. On cutting open the tube, warty or polypoid excrescences, white to yellow brainlike nodules, or a combination of both are found. The lumen and abdominal ostium remained patent in three cases. Janvrin's case is the sole one reported in which the origin was from the musculature and in which the growth concentrically surrounded the tube lumen. All others arose from the mucosa.

Microscopically, two cases each of spindle- and round-cell sarcoma, one myxosarcoma, one myosarcoma, one combined spindle- and giant-cell and three peritheliomata (perivascular sarcoma) are recorded.

The cases reported in short résumé are:

Senger (167), 59 years old, bilateral, papillomatous and polypoid, metastases in Douglas's cul-de-sac. Round-cell sarcoma with glandlike inclusions. Autopsy finding.

Gottschalk (168), 37 years, unilateral, size of apple, tube pervious, retroperitoneal nodes enlarged. Both tumor and nodes showed small spindle-cell sarcoma.

Janvrin (169), unilateral, lumen open, myxosarcoma with embryonal connective tissue and unstriped muscle.

Sänger (170), 42 years, bilateral, papillary and diffuse. Small, round-cell sarcoma. Died in six months from metastases.

Jacobs, I (171), orange-sized tumor, myosarcoma.

Jacobs, II (172), 27 years, ascites, bilateral, soft, lobulated, sacral glands enlarged. Spindle-cell with myxomatous degeneration.

Scheffzek (173), 61 years, size of goose egg, soft, lobulated, fimbriae normal. Spindle and multinuclear giant cells.

Gosset (174), 44 years, unilateral, sausage shaped. Perithelioma (plexiform angiosarcoma).

Barbour and Watson (175), 53 years, unilateral, hard nodular (brainlike, necrotic), perithelioma. Died after operation. Metastases found.

Müller (176), bilateral perithelioma, no details.

The following cases are more doubtful:

Dixon Jones (177), three so-called "myelomas" of tube, no clinical data; description unintelligible.

v. Kahlden (178), cauliflowerlike growth.

Eglington (179), "mesothelioma."

The glandlike areas found by Senger (l. c. 167) and Sänger (l. c. 170) in their tumors may well have been folds of mucosa isolated and surrounded by the growth, as Sänger supposed.

SECONDARY TUBAL SARCOMA

Lockyer (l. c. 60, II, p. 734) reports a case of uterine perithelioma invading the tube by continuity. The writer operated upon a small round-cell sarcoma of the uterus involving the broad ligament and one tube. No statistics as to frequency of involvement of the tube from uterine sarcoma are available. For lymphosarcoma see Schlagenhaufer's case (Chapter VIII, p. 253).

Thaler (180) reports *leukemic infiltration* of both tubes in consequence of an acute myelo-lymphatic leukemia. The tubes contained streptococcic pus. Lymphocytic and myeloid cells infiltrated the tubal folds. The rest of the genital tract was uninvolved.

Schlagenhaufer (181) described two cases of Hodgkin's disease ("typus Paltauf-Sternberg") in which the tubes and ovaries were infiltrated and in one case substituted by a polymorphous granulation tissue with numerous large cells. Macroscopically the infiltrates were nodular and yellowish-white in color.

PARASITES

Ecchinococcus cysts are rare in the tube, and of primary cyst, according to Eden (182), only two beside his own are recorded (Péan, Doléris). The usual condition is ecchinococcus disease of the subperitoneal connective tissue of the pelvis, or general peritoneal dissemination with secondary development within the tubal lumen after the cyst has become adherent to the

pelvic organs. According to Young and Welsh (183), if the liver ecchinococcus ruptures, the daughter cysts gravitate into the pelvis, form adhesions there and spread throughout the abdomen.

In Doléris' (184) case the cyst was intramural, the tubal lumen being patent. Moloney (185) described a cyst which secondarily grew into the uterus and then burst into the tube. Cases arising from subperitoneal cysts with secondary involvement of the tube are reported by Daschkewitsch (186) and v. Kroph (187). Doléris (quoted from Bénoit, 188) found enormous distention of the tubes, 57 and 53 cm. in length. In Abramitschew's case (189) the distended tube caused dystocia.

The literature will be found in Bénoit (l. c. 188) and Taylor Young and Welsh (l. c. 183).

Oxyures vermiculares were reported by Moro (190) in a tube. Tschamer (191) found two worms in the unaltered tube in a specimen removed by hysterectomy.

Ascaris lumbricoides was described in a reddened tube by Bizzozero (192). There was a perforation in the rectum. Saint (193) found a dead worm in a pyosalpinx. Nacken (194) found a similar condition, the pyosalpinx adhering to a coil of ilium.

Tapeworm.—Danielson (195) found the head of a tapeworm in the right tube. The body was in the pelvis. He believes that a pyosalpinx perforated into the gut and that the tract later tore off.

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CHAPTER X

THE OVARY

The numerous gross and microscopical changes which occur under physiological conditions in the ovaries (infancy, childhood, puberty, menstruation, pregnancy, puerperal state and senility) have been described in detail in Chapters III and IV.

Some of the conditions classed as pathological are either entirely physiological or merely indicative of transient disturbances. Among these are cystic corpora lutea and so-called polycystic ovaries. For the sake of convenience these two subjects will be discussed in connection with simple cystic accumulations, and inflammations respectively.

CIRCULATORY DISTURBANCES

During coitus and menstruation the ovaries become temporarily engorged and increased in size. This is proved by observation on ovaries prolapsed in inguinal hernias (Theilhaber, 1).

The same causes that produce hyperemia, engorgement, localized or diffuse hemorrhage in the fallopian tubes (see p. 327) operate on the ovaries.

These conditions include stasis from general and local causes, hyperemia and toxic changes resulting from infectious diseases, obstruction of the circulation from traction of tumors, displacements of the uterus, torsion of the normal adnexa, torsion of ovarian tumors, strangulation or torsion in hernial sacs (especially in infancy) (Moschcowitz, Heineck, 2), thrombosis of the spermatic vessels and inflammations of the peritoneum. For literature see Fallopian Tubes (p. 328).

Very rarely varices at the hilus or angiomatous collection of vessels in the stroma have been noted (Gottschalk, Marchand, 3). Death from hemorrhage from a burst varix was reported by Hörnig (4).

Circulatory disturbance manifests itself first as hyperemia, next diffuse edema results (on section the cut surface oozes a clear or bloody fluid), and finally diffuse or localized hemorrhages occur. In extreme degrees of stasis the ovary is tense, blue-black and friable and may rupture upon the slightest touch (hematoma ovarii).

The bleeding commonly takes place into preformed cavities—follicles, corpora lutea or ovarian cysts. It resembles hemorrhages which occur

physiologically into some atretic follicles, and into all corpora lutea, but exceeds them in degree. Either a follicle or corpus luteum may rupture and the blood collect as a peri-ovarian or pelvic hematocele (Cohn, Urban, 5).

Death has occurred from such hemorrhages. It is necessary to exclude ovarian or tubal pregnancy by microscopic examination of the ovary and clots, but Forssner (6), who has analyzed 40 cases, goes too far when he claims that all such cases are ovarian pregnancies with complete extrusion of the ovum. The corpora lutea are those of menstruation. In Reinhard's case (7), in which tubal pregnancy existed, the hemorrhage must be ascribed to beginning tubal abortion, not to the corpus luteum. The bleeding may come from follicles (Primrose, 8), or rarely from a tear in the ovarian parenchyma (Roll, 9), it may be repeated in the same patient (Taylor, 10). Often a trauma—cough, heavy lifting, handling during operation (Ferguson, 11) may be considered as the direct cause.

In infectious diseases such as cholera, the hemorrhage is more often diffuse and in the stroma (Fränkel, 12). Petechial hemorrhage may also result during the operative removal of ovaries and these artefacts have been mistakenly interpreted as the result of or cause, for example, of uterine fibroids (Ohmann, 13).

In torsion of the adnexa the infiltration with blood may be so extreme as to cause obliteration of all structures. Adhesions commonly occur and the ovaries may eventually sclerose and atrophy.

Blood pigment, in various stages of absorption, in the stroma of the ovary, bears evidence to preceding hemorrhage.

CHANGES IN SIZE, SHAPE, POSITION, AND ABSENCE OF, THE OVARY

The shape and size of the ovary is affected by its functional condition. The presence of ripe follicles or one or more corpora lutea enlarge the gonad. In infancy and old age the ovary is small. Ries (14) especially, has pointed out that cystic corpora lutea may produce periodic ovarian swellings.

Elongation of the ovary may be produced by the traction of adhesions (Bovée (15), Fig. 255), bands and by pressure exerted by tumors. Pressure may flatten the ovary. The gyrate ovary shows many incisures, producing brainlike convolutions (Adler, Bien, 16).

Mechanical factors (bands, adhesions, torsion) may subdivide the ovary or partially split off small portions (Engström, 17) (*accessory ovary*) (Fig. 256).

Breaks in the continuity of the gonad may occur, so that two or more apparently discrete nodes of ovarian tissue result. They may be connected by bridges of ovarian stroma or be entirely discrete.

Supernumerary ovaries together with supernumerary tubes are due to a congenital excess (see p. 491).

The *position* of the ovaries is largely dependent upon the position of the uterus, as is that of the tubes (see p. 328).

Prolapse of the ovaries up to the sacro-uterine fold is regarded clinically as of the first degree, descent into Douglas' cul-de-sac as of the second degree. The clinical importance of non-adherent prolapse has constantly diminished. For literature see Ward (18), Kossmann (19).

FIG. 255.—ELONGATED OVARY DUE TO TRACTION EXERTED BY A PAROVARIAN CYST. Note gyrate ovarian surface and dilatation of the veins in the mesosalpinx.

Prolapse is most often due to retroflexion and puerperal subinvolution of the uterus.

Displacement of the ovaries by bands, tumors, exudate may lead to torsion and traumatic amputation.

Acquired absence of the ovaries, usually unilateral and often combined with absence of the tube, is rare. It may be due to bands from a fetal peri-

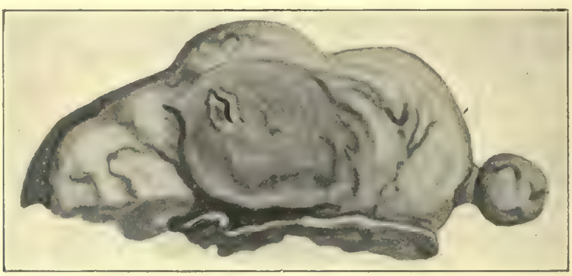

FIG. 256.—ACCESSORY OVARY. Attached to the main structure by a pedicle. Corpus Luteum in the main ovary showing stigma (point of rupture of follicle.)

tonitis (Busse, 20) or in later life most often results from torsion. The atrophic or calcified ovarian remnant may be found in Douglas' cul-de-sac (Ward, l. c. 18) or parasitically attached to any intra-abdominal organ, or the ovary may be absorbed without leaving a trace. Where other malformations coexist (as in Gellhorn's case (21), absence of the kidney on the same side) the aplasia must be considered congenital, in spite of a well developed uterus and normal insertion of the round ligament into the uterine horn. For literature see Kossmann (l. c. 4, p. 128), Sachs (22), Hauser (23).

HERNIA OF THE OVARY

Displacement of the ovary into the inguinal canal is most frequent (English, 24), although in women femoral hernia predominates. The gonad exceptionally forms the contents of an ischiadic, obturator or umbilical hernia.

Inguinal ovarian hernia in the young is probably most often congenital. In adult life such herniae occur in multiparae of the working class (Pfannenstiel, 25). The condition may be bilateral, in which case it produces sterility. Tumors may develop in the displaced ovary. The tubes most often accompany the ovaries in their descent, the uterus is likewise encountered (see page 176) and malformed uteri or pseudo-hermaphroditism is reported as a complication. The ovary as the sole contents of a hernial sac is least frequent.

Torsion and strangulation may occur.

INFLAMMATION OF THE OVARY

As in the discussion of other parts of the genital tract, only such changes as are due to bacterial infection will be considered as inflammations.

Nevertheless the degenerative changes described in some of the infectious diseases such as scarlatina, measles, diphtheria and cholera (hemorrhages in the stroma, cloudy swelling and degeneration of the follicular epithelia) may be inflammatory. In some of these diseases the bacterial cause is known, in others, as measles, not. Epidemic parotitis often causes ovarian involvement (Gentili, Brooks, 26).

Acute Oöphoritis.—Acute inflammation of the ovary results from invasion by the streptococcus, gonococcus, colon bacillus, typhoid bacillus and other organisms. No exact statistics as to frequency can be given as oöphoritis usually is diagnosticated clinically in connection with inflammation of the remainder of the genital tract. Only the fewest cases come to operation or autopsy.

Martin and Orthmann (l. c. 4, p. 215), of 45,213 patients, diagnosed oöphoritis in 5504, and of these only 110 were operated upon for suppurative conditions. In 70 fatal puerperal infections 10 showed phlegmonous oöphoritis. Inflammation is set up by gonorrhea, puerperal sepsis, instrumentation, by organisms invading from adherent intestine and being transported metastatically through the blood stream. The routes resemble those described under Salpingitis, p. 329.

In puerperal and also *operative infections* (including curettage, criminal abortion) the bacterial invaders may reach the ovary by the lymphatics, or the veins (thrombophlebitis) or both, in which case the inflammation begins in the hilus. More rarely the tube by direct contact infects the ovary on its surface, or a pelvic or general peritonitis causes surface infection.

In gonorrheal oöphoritis the infected tube almost invariably soils the neighboring peritoneum and ovary. Lymphatic or vein infection is the exception.

Oöphoritis due to surface invasion is facilitated by the rupture of follicles, the tear offering a point of entry. The blood in the follicle or corpus luteum supplies a good medium for growth (infections secondary to peritonitis, adherent appendix or intestine). Metastatic oöphoritis may originate from a distant focus—tonsillitis, parotitis (Wilder, 26a).

Macroscopic Appearance.—In the stage of hyperemia the ovary appears red, and loses its bluish pearly sheen. Petechiae and swelling supervene and if pus formation occurs in the lymphatic and thrombo-phlebitic types, yellowish streaks or minute multiple abscesses will be noted on sec-

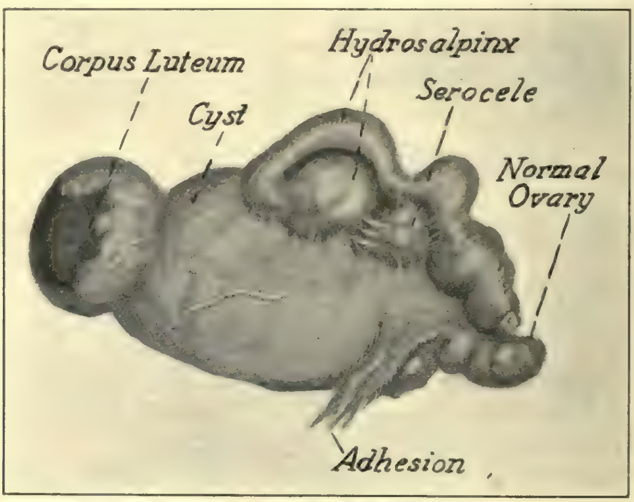

FIG. 257.—SUBACUTE OÖPHORITIS; WITH HYDROSALPINX ADHERENT TO THE OVARY. Serocele, small remnant of normal ovarian stroma, median cystic portion of the ovary, to the pole of which is attached a fresh corpus luteum. Notice the prominent vessels on the surface of the entire ovary due to peritoneal bands.

tion (extending inward from the hilus). In severe puerperal oöphoritis the organ may rapidly become pulpy and semifluid (oöphoritis dissecans). Localized abscesses either in unruptured or ruptured follicles and in corpora lutea may form, or one or more abscesses may develop in the stroma. Commonly the tube is also involved, peritonitic adhesions rapidly form (perioöphoritis) and, especially in puerperal conditions, the infiltrated broad ligament, accumulations of intraperitoneal fluid (seroceles), together with tube and ovary form a single large (or bilateral), friable, readily bleeding mass amid adherent intestine. (Fig. 257.)

The outcome is various. In severe puerperal infections, in which the oöphoritis plays but a minor rôle, fatal peritonitis, pyemia or bacteremia may develop. In mild puerperal or in gonorrheal cases encapsulation of the

inflamed ovary by adhesions may produce adherent ovaries, or in severer infections may be followed by complete atrophy and sclerosis with disappearance of the follicular apparatus.

Pyovarium.—Localized abscess may form either in follicles, corpora lutea, or diffusely occupying the ovary. These abscesses may absorb, leaving merely scars, or may calcify or become sterile. They may attain huge size (that of a man's head). The abscess may rupture into the free abdominal cavity, producing diffuse peritonitis, or into the bladder, intestine, vagina or externally through the abdominal wall.

By agglutination to the tube, an ovarian abscess may form a conglomerate mass. By absorption of the intervening septa a *tubo-ovarian abscess then develops.*

Of Martin's and Orthmann's 100 cases of pyovarium (l. c. 4, p. 227), 23 were bilateral, 22 were puerperal and 12 the result of intra-uterine manipulation. Only 17 of them were unaccompanied by salpingitis. Of 55 cases, 20 were sterile. The gonococcus was found in 15, streptococcus in 8, staphylococcus in 1, colon in 2 (Menge, 27). Hunter Robb (28) found the bacillus proteus.

Corpus Luteum Abscess.—Twenty-one of Martin's cases were corpus luteum abscesses. Chomé (29) reported 17 of non-puerperal origin, Wiener (30) one, the size of a grapefruit, containing hemolytic streptococci. His patient was a virgo (metastatic origin). Large abscesses probably form only in corpus luteum cysts.

The corpus luteum abscess is recognized by its nodular, crenated, yellow wall. The lining can readily be pulled off. The lining may, however, be destroyed in places or entirely, and replaced by an ordinary pyogenic membrane. Moreover, a yellow membrane due to pseudoxanthoma cells found in chronic suppuration (*vide* Histology) may prove misleading.

Microscopic Appearance.—The mode of origin may be evident in some cases. Peritonitic (often appendicular) origin may document itself by adhesions on the surface and involvement mainly of the periphery. Small multiple abscesses in the stroma bespeak a lymphatic invasion.

Stroma.—Dilation of the vessels (Fig. 258) is noted in the early stage of hyperemia. This is followed by edema and hemorrhage. Leucocytic and round-cell infiltration along the vessels and about the follicles appear. In less acute infections and after the acme of the process has passed plasma cells abound. They are not limited to gonorrheal infections, as Wätjens (31) states.

In destructive processes necrosis and liquefaction may destroy all cell structure.

The follicles may show swelling and degeneration of the granulosa. The ovum may degenerate. The follicle contents in severe cases may be purulent. The extent and severity of the involvement of the follicles varies greatly.

Glandlike acini lined with cubical epithelium, may be found. They

result from down growth of the peritoneal epithelium, sometimes formed along fistulous tracts due to the discharge toward the surface of small abscesses.

The histology of a *pyovarium* depends upon the localization of the abscess. Abscesses in the stroma, or progressive abscesses originating in a follicle or corpus luteum but destroying the wall of the preformed vesicle, show granulation tissue composed of new formed capillaries, young connective tissue cells, leucocytes and fibrin.

The walls may have a yellowish tinge from the presence of *pseudoxanthoma cells* (Aschoff, 32) which are large, pale, rounded, connective tissue cells with a lightly staining round nucleus. They resemble lutein cells but do not extend sheetlike, appearing scattered among the lymphocytes, leucocytes, plasma cells and Russel bodies (Miller. 32).

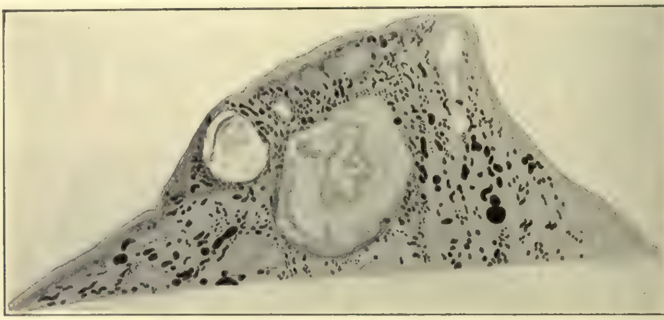

FIG. 258.—SHOWING AN OVARY REMOVED AT POST MORTEM FROM A CASE OF CRIMINAL ABORTION AT THE THIRD MONTH. (Low power.) Earliest stage of inflammation marked by dilatation and fullness of all the vessels, large and small. The specimen shows distribution of vessels around follicles and a corpus luteum.

Abscesses in lutein cysts are lined by sheets of lutein cells, separated from the contents of the abscess by a connective tissue membrane if the corpus luteum has reached an advanced stage (see Chapter III, p. 56) or, if developed from an early corpus luteum, lined by the unprotected lutein layer (Fig. 259).

The healed ovary shows scar formation; in severe processes sclerosis with diminution or absence of follicles, sometimes calcification. The perioöphoritic membranes appear as fine velamentous projections. Epithelial lined spaces parallel to the surface are common. Acellular areas, hyaline scleroses, large macrophages, often with pigment inclusions, are found (Meyer, 34).

"Chronic Oöphoritis."—To-day this is still in the stage that "chronic endometritis" was before Hitschmann and Adler clarified that subject.

As the result of slow healing, acute oöphoritis may reach a subacute stage, as the result of recrudescences, gonorrheal oöphoritis may flicker up in the course of repeated attacks of pelvioperitonitis. Ultimately the ovary

heals by scar formation, by restitution or sclerosis, or abscesses may persist (see p. 371) (Fig. 260).

The chronic oöphoritis of the authors corresponds to *microcystic* or *polycystic degeneration of the ovaries* (Pfannenstiel, l. c. 3), Martin and Orthmann (l. c. 4) without bacterial cause. Such changes are regularly found in the newborn (Delestre, Gaifami, 35), have been described as specific in status lymphaticus and thymo lymphaticus (Bartel and Herrmann, 36) and were regarded by Nagel (37) and Gebhard (38, p. 293) as physiological.

Davis (39) reports only 10 of 62 chronic oöphoritis cases (fibrocystic degeneration) sterile. He and Rosenow found streptococcus viridans in 50 per cent and the Welch bacillus in 33 per cent. A number of the

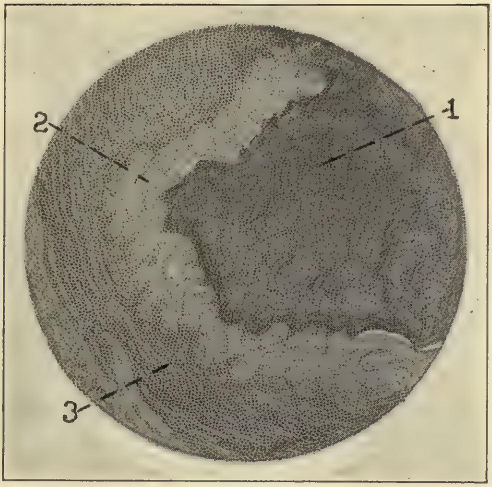

Fig. 259.—Corpus luteum abscess. (Very low power.) Convolutions forming wall of the abscess. 1. Fibrin and pus cells in center of the abscess. 2. Layer of corpus luteum cells, necrotic and regressing. 3. Round-cell infiltration surrounding the abscess and demarcating it from the ovarian stroma.

ovaries were removed incidentally with fibroid uteri. One cannot avoid questioning these results.

Microscystic ovaries appear as a congeries of numerous, tense, thick- or thin-walled follicles of pea to cherry size, which project above the surface and give the enlarged ovary a bossed appearance. On gross section the ovarian stroma may be reduced to mere septa (Fig. 261). The dilated follicles may contain normal or degenerated ova, and may be lined by a thinned-out layer of granulosa cells (Fig. 262). Not infrequently the granulosa may be wanting. Cystic atresia (Chapters III and IV, p. 59) is frequent. Corpora lutea are present in the ovaries of adults.

In certain animals, notably the sow, the writer has noticed that in pregnancy and near rut the ovaries form grapelike conglomerations as the

result of the development of many (3 to 5) corpora lutea and multiple cystic follicles. During the quiescent period the ovaries of the sow are small and solid.

This observation applies to some degree to the human ovary. An as yet undetermined stimulus (inflammation, according to R. Meyer) causes the ripening of numerous follicles which are arrested at various periods of

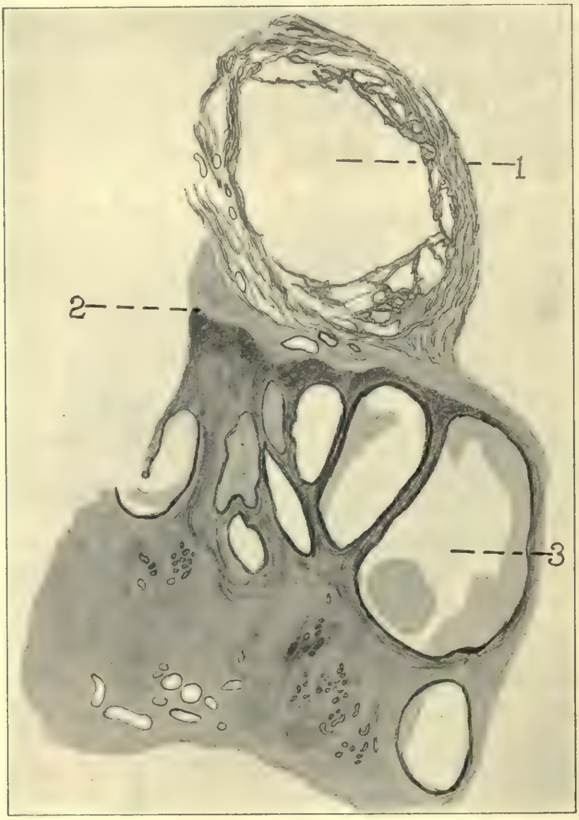

FIG. 260.—CHRONIC INFLAMMATORY TUBO-OVARIAN MASS. (Very low power.) Tube and ovary are agglutinated into a single mass distinguishable only on microscopic section. 1. Tube showing dilatation, and chronic salpingitis. 2. Junction of tubal and ovarian stroma. 3. One of several follicular cysts of the ovary.

development by the inhibitory action of the corpus luteum (see p. 82). The microcystic ovary results.

In a large per cent of cases with chorionepithelioma, and in one instance in the presence of a fetus harboring a teratomatous growth (40), *polycystic lutein changes* occurred in the ovaries. Here not only does the cystic enlargement of the follicles reach an exaggerated degree but overgrowth of the theca lutein cells takes place (see p. 380). Regression with *restitutio ad integrum* is frequent after emptying of the uterus. In other

words the stimulus, which in these cases is recognizable, may consist of an excessive amount of overactive or possibly altered chorion epithelium.

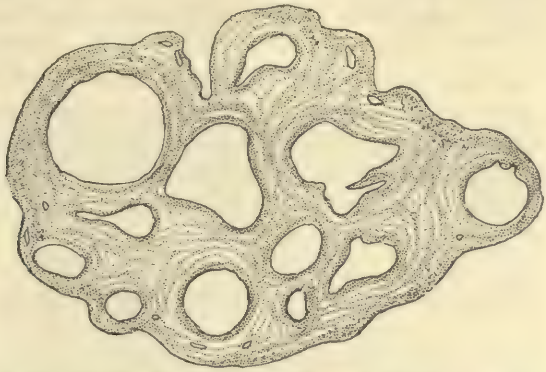

FIG. 261.—OVARY WITH CYSTIC CHANGES. (Very low power.) Shows numerous cystic follicles due to rapid maturation and atresia. This may be a transitory functional stage.

We cannot agree with Reynolds (41), who finds different types of mature follicles and corpora lutea in the ovaries of fertile and sterile women, and must interpret his "types" as various normal stages of atresia and

FIG. 262.—POLYCYSTIC OVARY. (Low power.) Higher power of the condition similar to that shown in the preceding figure, showing numerous cystic cavities lined by thinned-out layer of granulosa cells (called "cystoma follicularis" by some and "cystoma serosum simplex" by others).

corpus luteum formation. Nor can we agree with Schochet (42), who, (by means of the Abderhalden reaction) concludes that follicle rupture is due to a proteolytic enzyme, which is absent in "fibro-cystic" ovaries. Perhaps

the enzyme is absent. If so, it is because these follicles are atretic and no longer active.

In some instances peri-oöphoritic adhesions may produce a moderate degree of polycystic "oöphoritis." Usually sclerosis and atrophy ultimately supervene.

Temporary sterility may result from polycystic ovaries. Observation at re-operations, when such opportunities arise, should be utilized to determine whether the condition is not transitory as the writer surmises. Ignipuncture and resection do not affect the underlying cause which produces the simultaneous ripening of numerous follicles.

TUBERCULOSIS OF THE OVARIES

What has been said concerning the mode of infection in tuberculosis of the tubes applies with slight modification to this disease in the ovary (see p. 340).

Extension by continuity is most frequent, as shown by the almost invariable presence of either tuberculosis of the peritoneum or other genital organs or both. Schlimpert (43) found the ovary involved alone, only once in 73 cases of genital tuberculosis. Ovarian tuberculosis in his series formed 13.7 per cent of genital tuberculosis, 14.5 per cent in Merletti's series (44) and 15.9 per cent of Orthmann's (l. c. 4, p. 356) collected series of 307 genital tuberculosis diagnosed *macroscopically*. In a second series of 103 cases in which the microscope was used the percentages more than doubled, 33.9 per cent.

Whitman and Greene (45) report tuberculosis (caseous) of the ovary in a stillborn child.

The disease was bilateral in 7 of Schlimpert's cases (l. c. 43) and unilateral in 3.

The ovary may appear normal to the eye. More often it is enlarged and embedded in dense, keloidal adhesions, or studded with tubercles. In advanced disease, caseating areas (diffuse, multiple or central, pyovarium) with thick, ragged wall are found. The tuberculosis may be limited to a follicle, corpus luteum, corpus luteum cyst or ovarian cyst.

Lampert (46) describes a corpus luteum abscess containing mixed infection, streptococci and tubercle bacilli.

In Fullerton's case (47) a tubo-ovarian abscess contained tubercule and typhoid bacilli.

The literature covering tubercular infection of ovarian cysts is voluminous. Celler (48) in 1904 was able to collect 13 undoubted cases. Forgue and Chauvin (49) in 1919 found 35 cases. Adenocystomas (Brons (50) and dermoid cysts (Cohn, 51) may be affected. The tuberculosis is usually spread by continuity from the peritoneum.

The histology of ovarian tuberculosis is simple. In the early stages

discrete tubercles are found in the superficial layers of the ovary (Fig. 263). Later, caseation supervenes. If a follicle (l. c. 51), corpus luteum or ovarian cyst is infected, the tubercular lesions are found in the wall of the preformed structure. The entire ovary may be converted into a mass of smeary detritus bounded by old adhesions.

FIG. 263.—TUBERCULOSIS OF THE OVARY. (Medium power.) On gross examination the enlarged adherent ovary appeared studded with minute abscesses. Note the absence of surface epithelium at the top. The stroma is infiltrated with round cells and epitheloid cells. At the lower left-hand corner hemorrhage into the stroma is shown. Above this is a typical tubercle containing a large giant cell. In areas not shown caseation was noted.

SYPHILIS OF THE OVARIES

What has been said in regard to syphilis of the tubes (p. 347) applies equally to the ovaries. None of the older cases are conclusive.

The cases of Hoffmann (52) and Gellhorn (53) show gummata of the ovary as part of a widespread diffuse gummatous invasion.

In Gellhorn's case the gumma was centrally located in the ovary. It was a granulomatous mass containing large numbers of plasma and eosinophile cells.

ACTINOMYCOSIS

Actinomycosis of the ovaries is a rare disease. Robinson (54) was able to collect only 16 cases, to which at least three more may

be added (55). Almost invariably other abdominal organs, especially the intestine, are involved. The ovaries form moderate sized tumors, often involving the tubes also (see p. 347), embedded in adhesions, granulation tissue and fistulous tracts leading to the appendix, rectum or adherent small intestine.

On gross section the ovary appears spongelike or honeycombed by innumerable small fistulous tracts filled with yellow pus in the early stage, or changed into a necrotic pus sac in advanced disease. Around the granulation tissue the stroma contains plasma cells, leucocytes and pseudoxanthoma cells. Mycelia of the ray fungus are found (hyaline masses radiating from a common center, with club-shaped ends), amid granulation tissue or necrotic debris.

The point of entrance is hard to determine. Schiller (l. c. 55) believed that in his case decayed teeth afforded entry, Grainger-Stewart and Muir (56) a fistulous tract leading to the vagina. Usually the intestine appears to be the starting point.

RETENTION CYSTS

Follicular Cysts (*"hydrops folliculi," Cystoma serosum simplex of Pfannenstiel*).—During the process of atresia one follicle may gradually increase in size and continue to distend until large dimensions are reached. Usually the resulting cyst is solitary, of walnut or lemon size, but a cyst containing 17 pounds of fluid has been described (Olshausen, 57).

Ordinarily, that portion of the cyst projecting beyond the ovary is whitish, parchmentlike and thin walled. In larger cysts, remains of the ovary may be found in some portion of the wall. The inner surface is smooth and glistening, only rarely are localized, flattish papillations noted. The fluid content is never viscous and usually is colorless, or may be brownish or blood tinged. It is of low specific gravity, 1.005 to 1.026, and contains much albumen (Gebhard, l. c. (38), p. 313).

The histology of the cyst wall is simple. The main constituent is a lamellated fibrous layer of varying thickness containing a moderate number of blood vessels running parallel to the lining membrane. This lining is usually a single layer of low cylindrical epithelium with central, darkly staining nucleus (Fig. 267A, p. 389).

Many cysts have lost all epithelial lining. In some the epithelium is low, darkly staining and devoid of cell boundaries—syncytial (Pfannenstiel, 58). In some small cysts derivation from the follicle can be traced by the fact that theca lutein cells (see Chapter III, p. 51) are found persisting in the cyst wall (Fig. 267B).

Occasionally low, flat and broad papillations may be found on the inner surface (Fig. 267C). They are rarely widespread and show merely the same

epithelium upon a broad connective tissue stalk. All evidence of adenomatous gland formation, such as is regularly seen in the walls of pseudomucin cysts or serous cysts are wanting.

Pfannenstiel considers this type a proliferating neoplasm (l. c. 58, p. 128). He derives it from the follicle. v. Kahlden (59) derives the origin from the surface epithelium of the ovary. The frequency with which transitions from atretic follicles can be traced, inclines the writer to the old view of simple retention cysts, which, as elsewhere in the body, may reach large proportions.

Corpus Luteum Cysts.—The involution of the corpus luteum has been described (p. 57). Almost half of all the yellow bodies at some stage develop a cystic cavity. However, it is comparatively rare for cysts of perceptible dimensions to form.

The resulting cysts are usually solitary. They are regularly more thick-walled than follicular cysts. The lining membrane, which is yellowish to bright orange-yellow, may be smooth, wavy, crenated or bossed. It can readily be pulled off from the connective tissue wall. The content of the cyst has a yellowish, brownish or reddish tinge, depending upon the amount of lutein and blood pigment present. The fluid may be thin to syrupy in consistence (Pitha, 60). This author describes a cyst the size of a child's head, with lutein membrane and pseudopapillary elevations. The lining of the cysts are formed most commonly of a thin layer of connective tissue covering over a typical layer of pale epithelioid lutein cells, forming a crenated border with capillary network between the cells (see p. 55, Chapter III, Fig. 43).

This distribution is often wrongfully interpreted as loss of the inner epithelial lining and preservation of the theca lutein cells. However, as will be noted on page 56, the granulosa lutein cells are regularly covered by the fibroblasts which grow in from the central blood clot (see Fig. 43, p. 55). This arrangement is most often observed in cysts.

Occasionally the unprotected lutein cells form the lining. Their free border is irregular, feathered and uneven (Fig. 46, p. 57). They may be missing in spots, or the cyst may have no epithelial lining. A hyaline band may then border the cyst wall.

The cyst fluid contains swollen lutein cells, fat, detritus and cholesterin crystals.

In this connection other abnormalities of the corpus luteum may be mentioned.

Rokitansky (61) and Cristalli (62) describe corpora lutea pouting like prolapsed hemorrhoids through the follicle rent. The surface may be cleft and ragged.

Luppoff (63) reports *prolapse* or extrusion of the yellow body, which may be found connected with the ovary by a thin stalk or lie free in the cul-de-sac.

Calcification of the corpus luteum has been described. The calcification

may involve the central core or the lutein layer. For literature see Santi (64), Markoe (65).

Hemorrhage from a corpus luteum (p. 367), corpus luteum abscess (p. 371) and tuberculosis of the corpus luteum (p. 376) have been described.

Tumors both benign (fibromata) and malignant (sarcomata and carcinomata) arising from the corpus luteum have been reported. Their origin is more than doubtful. For literature see Santi (l. c. 64) and Williamson and Barris (66), who have collected nine cases which, according to these authors, might also be interpreted as of hypernephric origin or derived from the interstitial cells of the ovary (?).

Lutein Cystic Ovaries.—These were previously referred to under "chronic oöphoritis." In over 50 per cent of all cases of hydatid mole and chorionepithelioma (Runge, 67) this condition is found. The ovaries may attain large size and may later regress (Fränkel, 68). They may produce clinical disturbances such as incarceration of the uterus (Bamberg, 69).

The ovarian tumors are caused by agglomeration of many thin-walled cysts with brownish yellow lining, producing a gigantic polycystic ovary. Usually the condition is bilateral. The resulting mass appears like a polycystic ovary increased by five diameters or like a congenital cystic kidney.

Early stages show great increase in the theca lutein cells, widespread and rapid development of many follicles to the ripe stage, equally rapid cystic atresia and diffuse edema of the stroma. Many cysts lose their lining of granulosa cells. In smaller ones, a typical lutein border persists. The main bulk of the lutein changes result from the theca lutein cells, which appear diffusely distributed in the stroma as in the interstitial gland of animals (Wallert, 70) (Fig. 54, p. 63), but whose continuity with the wall of follicles can be traced in serial section.

These changes when analyzed are seen to consist of an overhasty growth and an exaggeration of cystic atresia of follicles, together with intensification of the lutein development. Pick (71) and Fränkel (l. c. 68) believe that the ovarian stimulus produces the changes in the ovum, Seitz (72) and others that the overgrowth of an active chorion epithelium causes the ovarian change.

As in a certain number of instances, after expulsion or removal of the mole, regression of the ovarian tumors occurs, it is permissible to await the outcome. Only if continued enlargement is noted is extirpation indicated (Fränkel, l. c. 68).

Fränkel (72a) records a case where transitory ovarian tumors developed under the stimulus exerted by a teratomatous fetus. After its expulsion the ovaries slowly returned to normal dimensions.

By agglutination with a distended tube, especially a hydrosalpinx, either follicular or corpus luteum cysts may form a conglomerate tumor (Fig. 260). If the intervening septa atrophy a *tubo ovarian cyst develops.* For details see p. 336.

OVARIAN TUMORS

Frequency.—New growths of the ovary occur in from 1.4 to 2.8 per cent of gynecological cases.

Pflaume (73), 140 cases in 4861 patients; Schmidlechner (74), 720 in 50,000 cases, Martin (l. c. 4, p. 368), 527 in 36,158 cases.

Age.—The occurrence at different ages was recorded by Olshausen (75) as follows in 1764 cases:

Under 10 years of age	61
20 to 29 years	490
30 to 39 years	499
40 to 49 years	372
50 years and over	342

Martin (l. c. 4, p. 370) found the maximum incidence in the fourth decade; Kelly (76) in both pseudomucinous and serous cystadenomata reports 42.5 years as the average. Doran (77) found a large ovarian sarcoma in a premature infant. Carcinomata, sarcomata and teratomata are found in infancy and childhood (Wiel, Donhouser, Parry, Lésage and Girault (78). Downes (79) summarizes the 76 cases of children under 10 years, showing that the incidence of malignancy has increased because now more often recognized—29 were dermoids, 21 simple or multilocular cysts and 36 malignant (sarcoma or carcinoma). Kelly and Sherwood (80) collected 100 ovarian tumors occurring in women over 70 years of age.

Martin (l .c. 4, p. 370) believes that the unmarried show a greater liability to ovarian tumors than the married, and that the tumors in them occur in the third instead of the fourth decade as in the married. Theilhaber (81) found that 40 per cent of his cases with ovarian cysts were nulliparous.

General Consideration.—Ovarian tumors have certain properties in common and irrespective of their constitution are liable to certain accidents such as torsion of the pedicle, hemorrhage, necrosis, rupture, parasitic existence.

In general, ovarian new growths are either cystic or solid. The former are more frequent. Combinations of cystic and solid tumors abound.

The cysts may be minute, so that the mass appears solid until sectioned; section may show a honeycombed tissue. On the other hand, cysts may reach huge dimensions. Often a main cyst with numerous daughter cysts in its wall and projecting into the main cavity, is found.

Papillations which may be small and velvety, narrow and villous, or broad and cauliflowerlike, may appear within the cysts. The papillae may be limited to small areas, diffusely spread over the entire wall, or completely fill the cyst lumen. They may perforate the wall and grow on the outer

surface of the cysts. All varieties of cysts (retention, pseudomucin and serous cysts) may harbor papillae (Figs. 264 and 265).

Rarely grapelike papillary tumors, which in shape resemble intra-uterine hydatid moles, occur (Klein, 82).

Although the clinical dignity (especially an increase in malignancy) of ovarian cysts may be markedly affected by the presence of papillae, these growths should not be used to classify ovarian tumors. Such classification must rest solely upon the nature of the epithelium covering the papillations.

FIG. 264.—EARLY BENIGN SURFACE PAPILLOMA OF THE OVARY. (Very low power.) This small excrescence was found on an otherwise normal ovary. The epithelium covering the surface of the vegetations is in single layer, low cuboidal.

Pfannenstiel (83), of 66 papillary growths, found 9 pseudomucinous, 28 serous cysts adenomas, 28 carcinomas and one mixed tumor (adeno-sarcoma).

When the stroma of the papillae is myxomatous, sagolike bodies result. Solid tumors may be hard (fibromata), or soft and friable as certain carcinomata and cellular sarcomata.

The size attained, especially by cystic tumors and among these particularly by multilocular pseudomucin cysts, may be colossal.

Zaccharias (84) reported a cyst weighing 132 kg. Bullit (85) collected 23 cases each weighing more than 100 pounds.

Fay (86) collected five cases each over 200 pounds. Even at the present time such tumors are still encountered (Harley, 87).

Solid tumors of 35 pounds have been reported (sarcoma).

The *shape* of cystic growths is globular if single, but bossed and irregular if many cysts of approximately equal size exist. *The color* is bluish to pearly white if the wall is thick. Thin-walled cysts may be blue, green, yellow, reddish, depending upon the nature of their contents.

FIG. 265.—ADENOCARCINOMA PAPILLIFERUM OF THE OVARY: SURFACE IMPLANTATION. (Low power.) The other ovary contained a cystic adenocarcinoma which had broken through its capsule. Note irregularity of the epithelium.

The pedicle of an ovarian tumor may be short or long, thick or thin. It is formed by the broad ligament, mesovarium and ligamentum ovarii proprium.

Pedunculated ovarian growths are not surrounded by a peritoneal investment. If the pedicle is long and thin the ovarian growths appear to be attached to the uterine horn.

Small pedunculated growths usually lie behind the uterus in Douglas's cul-de-sac. Dermoid cysts are found in the anterior cul-de-sac with surprising frequency. With increase in size the top of the growth finally extends into the false pelvis and abdomen. When the abdominal portion preponderates, the new growth, unless fixed by adhesions or incarcerated, either suddenly or slowly rises into the abdomen. This change of position

is almost regularly accompanied by a torsion of the pedicle through 90 (Freund, 88) which, unless the pedicle is unusually thick, tense and short, causes no circulatory disturbance.

Adherent growths, infiltrating neoplasms, and solid tumors may remain in the small pelvis.

Intraligamentous (subserous) development results when the direction of growth causes the tumor to separate the layers of the broad ligament. (See Fig. 331, p. 491.) The tube, usually much elongated, courses over the surface of the growth. Serous-cyst adenomata are most often intraligamentous.

Intraligamentous growths are recognized by the fact that large blood vessels course beneath the thin movable peritoneal layer which envelops the tumor. The uterus may be intimately fused with the mass after the broad ligament and parametrium have been invaded. Development into the mesosigmoid and mesorectum are not uncommon.

The writer removed a multilocular pseudomucin cyst which extended to the skin of the perineum. In another instance the development was retroperitoneal and had separated the folds of the entire mesentery so that removal was impossible but obliteration was obtained by marsupialization. Bilateral intraligamentous tumors may elevate and elongate the uterus greatly.

Pseudo-intraligamentous development results when an ovarian cyst grows behind the posterior layer of the broad ligament, pushing both layers of the ligament up and before it, and ultimately fusing with the covering peritoneum. In such cases two layers of peritoneum cover the tumor. The tube courses over the growth as in truly intraligamentous tumors.

Torsion of the Pedicle.—A frequent complication in ovarian tumors is torsion of the pedicle. Grotenfeldt (89) reported 83 cases, or 15.2 per cent; Wiener (90) 33 cases, 12.26 per cent; Frankl (91) 8.5 per cent. The varieties of tumors and the frequency of torsion are as follows:

	Grotenfeldt	Frankl
Fibroma	29.7 per cent	21.0 per cent
Simple cysts	21.3 " "	20.0 " "
Cystadenoma	18.4 " "	15.1 " "
Dermoid	17.2 " "	8.3 " "
Sarcoma	6.4 " "	12.5 " "
Carcinoma	4.0 " "	2.7 " "

Torsion may occur in children (Nagel, 92). It affects the middle-sized tumors especially. Right-sided growths turn from right to left (picturing the twist as a circular stairway, the left hand being on the inner or central axis as described by Schauta (93), left-sided tumors from left to right (Küstner's law, 94). The law, according to Pfannenstiel, applies in 85.7 per cent of all twists of the pedicle (Lippert (95) 81 per cent).

Retorsion or spontaneous restitutio is described by Grotenfeldt (l. c. 89) who collected seven cases and reported six additional ones.

The causes of torsion are variously ascribed to the movement of the intestine, the contraction of the abdominal wall, to straining, coughing, etc. The torsion may result slowly by a summation of minute growth impulses or may occur suddenly, as post partum, when the emptying of the uterus causes marked intra-abdominal changes.

Complete arrest of circulation may result from a twist of 180°, and may be of minor degree after 20 complete turns (Tauszk, 96), depending upon the length and thickness of the pedicle, the mode and rapidity of onset, and other factors. Holländer (97) recorded a twist of 25 turns.

Although ileuslike symptoms often develop in consequence of torsion, true ileus is rare. In Krömer's (98) case the pedicle, after twisting through 450°, encircled a loop of intestine. Gronarz (99) reports a similar case, Azà (100) strangulation of the transverse colon.

Secondary Changes.—As the result of torsion severe circulatory disturbances may arise including hyperemia, edema (bluish color, thickening of cyst wall or diffuse hemorrhage into solid tumors), hemorrhage into the cyst lumen and cyst wall, gangrene and rupture of the cyst. Immediate and sudden increase (often doubling) in size accompanies these changes. Adhesions almost invariably form and may nourish the cystic or solid growth, which eventually can become free and lead a parasitic existence attached to the omentum or parietal peritoneum. The cyst may become infected. Peritonitis may develop.

A cyst may be torn loose from its pedicle, as happened in one of the writer's cases during transport to the hospital. Free hemorrhage resulted.

Rarely simultaneous torsion of bilateral ovarian cysts has been noted (Armstrong, 101). The uterus may be twisted (see p. 177), seen especially in the aged, in infancy and in the puerperium.

Hemorrhage (see p. 366) into ovarian tumors regularly occurs at the stage of torsion where the venous return is cut off, but the arteries still succeed in pumping blood past the obstruction.

Gangrene results where the blood supply is completely cut off and adhesions do not afford adequate nutrition. Infection and peritonitis then follow.

Most often as the result of necrosis, *calcification* and even *bone formation* may take place in ovarian tumors, especially in the walls of cysts. The entire cysts (dermoids especially) may calcify. Pfannenstiel (l. c. 83, p. 126) in the ovary found a stone the size of a pigeon's egg loose within a cavity lined by epidermis.

Cholesterin is frequently found in the cyst fluid, and is even macroscopically recognizable by its glitter (Fig. 266).

Rupture of ovarian cysts is reported frequently. The cause may be traumatic (vomiting, examination, labor) or spontaneous. The erosion by malignant growths into adjacent viscera is not included. Solid tumors rarely rupture (sarcoma, carcinoma; Amann, 102).

Wiener (l. c. 90), in 240 cases, found ruptured cysts in 5, or 2 per

cent. Düffner (103), in 363 cases, found the following regions involved—peritoneum 211, gut 51, externally 34, genital tract 33, bladder 26, two organs 8. Martin (104) reports pressure atrophy causing multiple perforation by a non-malignant growth (pseudomucin cyst) into bladder, rectum, ileum and sigmoid.

Rupture into the abdominal cavity may cause diffuse peritonitis. In pseudomucin cysts pseudomyxoma of the peritoneum (see p. 393) may follow. Hemorrhage may result and may cause death (Boldt, 105).

Infection of ovarian cysts is not an uncommon occurrence. Wiener (l. c. 90) in 240 cases found 6, or 2.33 per cent.

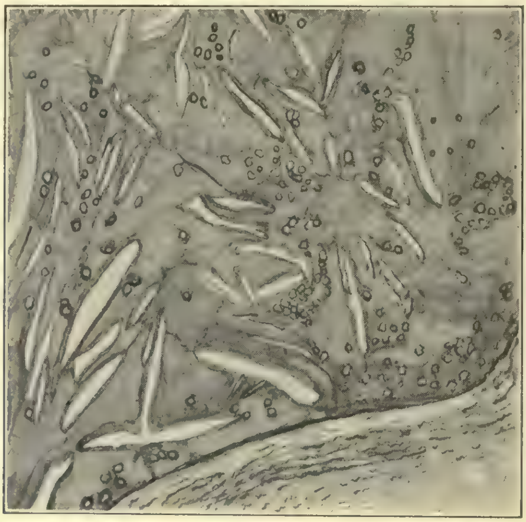

FIG. 266.—OVARIAN CYST WITH CHOLESTERIN CRYSTALS. (Low power.) Below is the cyst wall; then above, dark coagulated cyst contents with clear spaces formerly occupied by the cholesterin crystals, dissolved out during the preparation for sectioning.

Infection may occur through the circulation, through adjacent organs by continuity or contiguity, or may be introduced from without as by puncture (tapping).

The streptococcus (Cumston (106), Wiener, l. c. 90), staphylococcus (Tiburtius, 107), pneumococcus (Rissman, 108), gonococcus (Brettauer, 109), tubercle bacillus (Coe, 110), Celler (l. c. 48), etc., typhoid bacillus (Werth, Taylor (111), Coe, l. c. 110), colon bacillus (Menge, 112), have been found.

Dermoid cysts are most often affected because their contents offer a good culture medium. The complication is serious, as is shown by one death in six cases (Wiener, l. c. 90). Infection may occur late, as months after an attack of typhoid, or early, as a few days post partum. Gas was found in an infected cyst by Chavennez (113).

Rarely ovarian tumors are found in hernial sacs (inguinal, femoral, umbilical). For literature see Cullen (114). Barrows (115) described a

dermoid delivered through the rectum and anus in front of an advancing head (forceps; pelvic floor and rectum torn).

Parasitic growths result when tumors or cysts form nutrient adhesions in consequence of torsion of the pedicle. The pedicle subsequently atrophies and all nutrition is then derived from the adherent omentum, peritoneum, intestine, etc.

Truesdale (116) reported a parasitic cyst weighing 90 pounds.

In Pregnancy.—This complication is mainly of clinical interest. Fertility is reduced, especially by bilateral ovarian growths. Abortion occurs spontaneously in a high percentage of cases. Before the operative era, rupture of the uterus or of the tumor was of frequent occurrence during labor. In the puerperium gangrene from pressure incurred, or from torsion of the pedicle, or infection of a cyst with consequent peritonitis, is unduly frequent.

Slow-growing tumors such as dermoids and pseudomucin cysts are most often found. Grosse reports 53 bilateral oöphorectomies with 25 per cent of abortion in the first two months, 11 per cent the third and 12 per cent in the fourth. In spite of these figures he still expresses doubt as to the importance of the corpus luteum early in nidation (see p. 81).

For literature see Pfannenstiel (l. c. 3, IV, p. 443), Barrett (116a).

As a general rule, irrespective of the nature of the ovarian growth (except in manifestly inoperable malignant conditions) the tumor should be removed by laparotomy as soon as discovered. In the early months it is wise to wait until after the second month (in order to avoid removing the corpus luteum too soon). Toward the end of gestation full viability may be awaited and Cesarean section performed at the time of oöphorectomy, if indicated.

Arising from Supernumerary and Accessory Ovaries.—Only six cases of ovarian tumor originating from a *supernumerary* ovary (i.e., a third ovary accompanied by a third tube) are on record (Frank, 116b).

The one described by the writer was a papilliferous serous cyst adenoma situated on the external iliac artery. (See Malformations, p. 491.)

Thirty-six cases of tumors in accessory ovaries (ovarian fragments situated intra- or retro-peritoneally) are recorded (Stolz, 117).

Classification.—No satisfactory classification of ovarian tumors has ever appeared. Yet almost every investigator has at least added some modification of his own. This applies especially to classifications based upon histogenesis.

The authors are agreed in separating epithelial from connective tissue growths. Wilms (118) has thrown light upon the origin of embryoid or teratoid tumors, but the origin of simpler epithelial growths is still a matter of speculation and dispute. Ribbert (119) considers that pseudomucin cysts are embryomata in which only the entodermal layer has developed, the cyst representing rudimentary intestine.

To mention only a few of the early theories, Virchow (120) believed

ovarian cysts arose from connective tissue. Wilson Fox (121) and Waldeyer (122) derived their origin from the graafian follicle. A wolffian (parovarian) genesis was championed by Olshausen (123), Doran (124) and Clark (125). Marchand (126) believed that the fimbria ovarica frequently was continued to and into the ovary supplying areas of ciliated epithelium.

Lücke and Klebs (127), and Waldeyer (l. c. 122), and later Williams (128), referred epithelial tumors to the germinal epithelium of the ovary. This theory with various modifications and additions has gained ground. Pfannenstiel (l. c. 3) divides the tumors into "parenchymatous" and "stromatogenous" and brought about a distinct advance in definitely separating pseudomucinous from serous cysts by means of the chemical differences in their contents.

Robert Meyer (129) has extended the classification along these lines, dividing epithelial tumors into pseudomucinous and serous growths, but the writer cannot follow him when he extends this classification to carcinomata of the ovary, as these tumors rapidly lose all traceable resemblance to a pseudomucinous or serous origin.

Goodall (130) in a painstaking embryological study has attempted to show that all embryonic remains in the ovary including the medullary cords and the rete ovarii (see Chapter III, p. 65) are down growths of the surface or germinal epithelium and therefore not derived from wolffian ingrowths. This would signify that, no matter from what part of the ovary epithelial growths arise, *they all originate from the germinal epithelium.*

The structures which come into question are the ova, the granulosa cells, corpora lutea, medullary cords, rete ovarii, germinal epithelium, and, for those who agree with Lane-Claypon as to an epithelial origin of the interstitial cells, the interstitial cell.

Recently R. Meyer (131), after Liepmann (132) and others had appeared to have put a quietus on Gottschalk's "folliculoma" (133), has revived the origin of some tumors from the follicle cell. (See p. 402.)

All the research of the past has given no certain results. The writer therefore is forced to classify tumors upon a morphological basis.

Epithelial Tumors.—Of the adenomatous tumors one can distinguish the *pseudomucinous* (cystoma glandulare) by means of the chemical properties of the pseudomucin contents and the clear, high, nonciliated epithelial lining resembling the cells of the cervix (Fig. 267D).

The *serous adenoma* on the other hand has a highly albuminous contents and is lined with ciliated epithelium resembling that of the uterine body (Fig. 267E). Both varieties show marked tendency to cyst formation. In both, papillary growths may develop within the cysts or on the surface. Rarely macroscopically solid tumors are found, but no matter what gross variations are noted the chemical properties of the secretions and the microscopic characteristics of the cells run true to type.

These two types of adenoma, or better, cystadenoma, may also show carcinomatous changes, and the resulting adenocarcinomata may for a time plainly bear the hall marks of their derivation. Often, however, adenocarcinomata no longer bear evidence which makes it possible to refer them to either the pseudomucin or serous group. In no case is such relationship traceable in the solid cancers.

Besides pseudomucinous and serous adenomata, carcinoma will be considered. Embryonal tumors including dermoid cyst and teratomata will also be discussed.

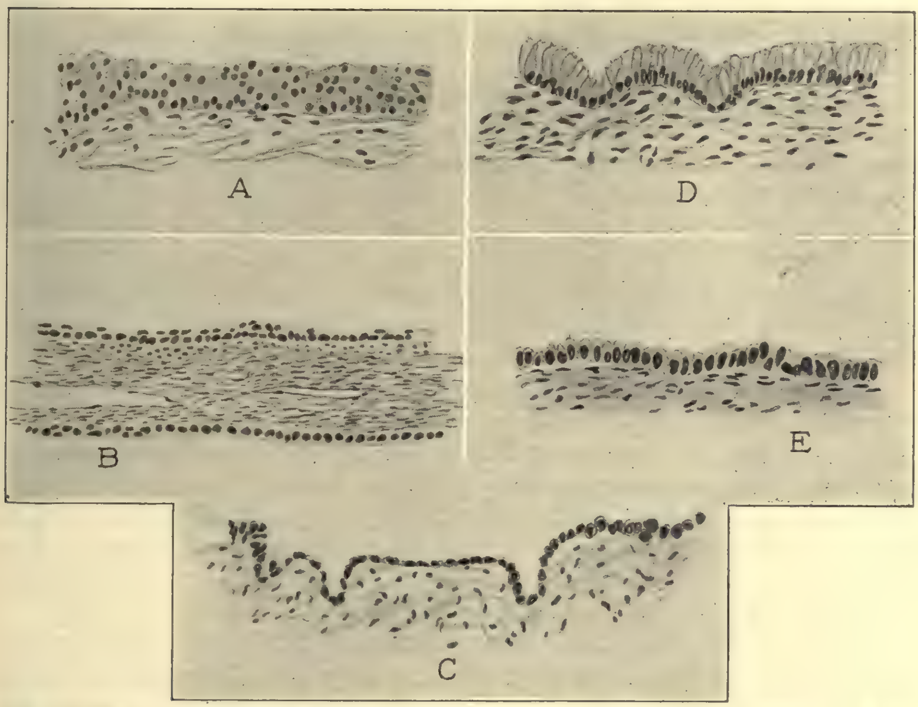

FIG. 267.—EPITHELIA LINING VARIOUS TYPES OF OVARIAN CYSTS. (High power.) A. Follicle cyst ("Hydrops folliculi," "cystoma serosum simplex of Pfannenstiel.") B. Simple ovarian cyst—a septum separating two contiguous cysts. The upper membrane appears to be of follicular origin as theca interna cells are situated below the lining layer. C. Benign Papilloma—single layer of low cuboidal cells. D. Pseudomucin cyst—high cuboidal epithelium resembling cervical epithelium (except for absence of cilia.) E. Serous cyst—dark, irregular, ciliated low epithelium. This type verges on the malignant.

CONNECTIVE TISSUE GROWTHS.—These include fibroma, fibromyoma, and sarcoma. Some authors recognize endothelioma and mesothelioma.

To a greater extent than elsewhere in the genital tract, ovarian tumors, histologically benign, show a tendency to dissemination (peritoneal), to wound implantation, and to the formation of ascites.

Peritoneal Implants.—Pseudomucin and serous cystadenoma after rupture, or when papillae grow on their external surface, may produce

innumerable small or large cysts on the peritoneum of the pelvis and throughout the abdomen, on all the viscera.

In some instances more solid nodules, grossly indistinguishable from general abdominal carcinosis, develop. After removal of the primary growth such implants may completely disappear. Pfannenstiel (l. c. 83) was able to collect ten such cases. More often they continue and sooner or later cause death by mechanical interference with the functions of the abdominal organs.

After rupture of a dermoid cyst, foreign body peritonitis resulting in the encapsulation of fat, hair and similar particles, may produce *pseudometastases,* nodules grossly resembling the implants above described (Pfannenstiel, l. c. 83, p. 119).

Wound Implantations.—In the small puncture wounds resulting from aspiration of ovarian cysts, as well as in the abdominal scar remaining after laparotomy, cystic or solid tumors have developed. The tumors have appeared after a few months' to many years' interval (21 years, l. c. 134) and either proved identical with the primary growth or have shown malignant changes. For literature see Olshausen, Schroeder, Polano (134).

Ascites occurs in 18.47 per cent of benign ovarian neoplasms, although in fibromata the percentage (72.73 per cent) far exceeds that of even malignant new growths (64.34 per cent, Lippert, l. c. 95).

The fluid may be due to the irritation produced by peritoneal implants. When the cause is removed the ascites disappears.

From what has preceded it has become evident that the dividing line between benign and malignant growths is hard to draw. As elsewhere in the body infiltrative growth, blood and lymphatic metastases taken together with the usual histological criteria of malignancy characterize malignancy. Yet carefully examined pseudomucin tumors have been known to produce lung metastases (Nicholson, 135).

In the case of malignant tumors, however, what is the great exception with benign growths becomes the rule. Peritoneal dissemination, local, regional and general metastases are frequent, ascites regularly appears and cachexia is noted.

Pseudomucin Cyst Adenoma.—This variety is the most frequently occurring ovarian neoplasm (Pfannenstiel (l. c. 3, p. 144), 75 per cent of ovarian cysts; Lippert (l. c. 95), 53.6 per cent of 638 ovarian tumors). It is usually unilateral (Pfannenstiel, 83 per cent; Lippert 88.9 per cent, except the papillary tumors of which only 50 per cent are unilateral). 9.65 per cent were found to be intraligamentous (l. c. 3). The size may be collossal (see Zaccharias, 84; Fay, 86, etc., p. 382).

Gross Appearance.—The tumor most often appears as an irregular, multilocular agglomeration of cysts. If large, a globular shape is given to the whole by the preponderant cyst; if small, bossed irregularity is common. Parvilocular tumors may appear honeycombed or solid. The surface is firm, smooth, glistening. Thick-walled cysts are white. Thin-walled cysts

allow their white, yellowish, greenish or brownish contents to shine through. Large veins course over the surface, especially in intraligamentous growths.

On cutting across a tumor it will be found composed of a few or many thin-walled cysts. Often the smaller ones project partly or entirely into the lumen of the larger ones. Frequently microcystic areas form semi-solid nodules. Rather infrequently papillary projections (velvety or like sago or rice grains) are found lining the inner wall. Spurs and septa due to partial atrophy of adjoining cyst walls are of frequent occurrence.

The contents in small and medium-sized cysts is a colorless to whitish, gelatinous, mucoid material resembling the vitreous humor of the eye, and is traversed by semitransparent strings and bands, the remains of atrophic septa. Occasionally a semi-solid gel is encountered, while in larger cysts the contents is regularly more fluid, cloudy and flocculent. Different colorations due to blood pigment (brownish), cholesterin (greenish) and fat (yellowish) can be noted. Pseudomucinous "grapelike" cysts, in which a large number of separate pedunculated cysts are bunched together forming a hydatidlike agglomeration, are very rare. Meyer (136) describes such a case. The epithelium within each cyst was typical.

The chemical composition of the cyst fluid has been studied by Hammersten (137). He showed that what Scherer had called "metalbumin" was a mucin derivative, while "paralbumin" was pseudomucin mixed with serum albumin.

Pseudomucin is composed of C, H, N, S and O. It is soluble in water, precipitated in long fibrinlike strands by alcohol and redissolves in water. Acetic acid does not affect pseudomucin, though this reagent precipitates mucin. Boiling with mineral acids liberates a reducing substance (reducing copper sulphate in alkaline medium). This shows that pseudomucin is a glycoproteid.

Pfannenstiel (l. c. 3, p. 147) calls the above pseudomucin "α" and says that its specific gravity is 1.025, its reaction alkaline. He finds in certain types of thin-walled cysts a more jellylike substance which he called pseudomucin "β." This gel is insoluble in water but is soluble in concentrated alkali. Its nitrogen content is very low.

A third type, pseudomucin "γ," is always fluid, very soluble in water, has a high nitrogen content and is but weakly alkaline (138).

Microscopical Appearance.—The cyst wall is composed of an outer fibrous layer, a middle cellular fibrous area and an inner lining of a single layer of high cylindrical epithelium resembling that of the cervix or intestine, but devoid of cilia (Fig. 267D, p. 389).

The outer layer has been compared to the albuginea of the ovary. The middle layer not infrequently resembles unstriped muscle.

The epithelium is a high cylindrical one with basal, narrow, darkly staining nucleus. The cells are in single layer and absolutely regular. The peripheral part of the cell is glassy, near the base it is granular. Mucicarmin stains the protoplasm. Goblet cells are common (Fig. 268).

Septa, spurs, pseudopapillae are found projecting into the lumen. Glandlike alveoli may occur in the walls, but usually even small alveoli begin to dilate early and form small cysts. In large cysts the epithelium may be low cuboidal.

True papillae may fill the lumen of the cysts. The epithelium is as described above. This applies as well to the rare occurrence of pseudomucinous surface papillations, which usually are due to penetration through the cyst wall of papillae growing within the cyst cavity.

RESULTS AND CURES.—Of 211 cases Pfannenstiel (139) reports that four died of recurrence, or 1.9 per cent. Death usually is due to symptoms

FIG. 268.—PSEUDOMUCIN CYST OF THE OVARY. (High power.) Convoluted wall of a pseudomucin cystadenoma showing the high cylindrical epithelium. Goblet cells occur. Pseudomucin and débris is shown in the lumen. The epithelium lies upon a dense connective-tissue stroma.

resembling those of abdominal carcinosis. Cures therefore approach 98 per cent (Glockner (140) 94.4 per cent). Papillary cystomas are more malignant, only 75 to 85 per cent remaining permanently well.

Incomplete operations never are followed by disappearance of the tumor rests. In five cases of Pfannenstiel two died, and three showed advanced involvement of the pelvic tissues. The course is usually slow.

Scar implantations are infrequent. Schröder (141) collected six, due to pseudomucin cystomas in which the recurrences were of the type of the primary growth; Polano (142), seven, in which the tumors of the abdominal wall were malignant. The question has been raised as to whether the original tumors did not contain carcinomatous portions.

Implantations due to rupture of thin-walled cysts (pseudomucin "β"

of Pfannenstiel) or resulting from surface papillomas may produce small multiple cysts throughout the abdomen. Rarely, after removal of the primary ovarian growth such peritoneal implants disappear. More often a slowly progressive diffuse dissemination of pseudomucin, by means of the peristaltic movements of the intestine, spreads the colloid throughout the abdomen. If cell complexes are contained in the mass, these cells continue to produce pseudomucin in their new location. "Pseudomyxoma peritonei," as it was designated by Werth (143), results.

Pseudomyxoma peritonei is characterized by several processes which occur simultaneously. After rupture of an ovarian cyst or of a mucocele of the appendix (Fränkel, 144) a colloidal mass is poured out into the peritoneal cavity. Because of its physical qualities the peritoneum cannot readily absorb the gelatinous substance, which clogs the subperitoneal lymphatics. A foreign body peritonitis results (granulation tissue, giant cell and connective-tissue production, endothelial proliferation). The cellular elements produced by the peritoneum penetrate the inert colloid and form septa and encapsulated masses. If the source of supply is not cut off by removal of the primary focus, or if secreting cells are contained in the gel, incredibly large amounts of pseudomucin may be produced. Biggs (145) removed 350 pounds of this material in 12 operations in a period of 9 years before the patient died at the age of seventy-five.

In a majority of cases epithelial cells are contained in the pseudomucin mass. These cells continue to secrete, form gland complexes and cysts (Fig. 269). No invasive tendency is shown, the organs being wrapped (but not penetrated) in a jellylike envelope (Lewis, 146).

The writer saw an early case operated upon by Dr. J. Brettauer. Here a small mucocele of the appendix lay embedded upon a thin cake of frogspawnlike jelly in the right iliac fossa. No adhesions had as yet formed. Bailey's case (147) was similar.

Ultimately death results from mechanical interference with the function of the intestine, fecal fistulae, cachexia or exhaustion. A few cures are recorded after repeated operation—17 "recoveries" in 40 cases (Günzburger, 148).

The case reported by Nicholson (l. c. 135) is unique. Here a pseudomucinous cystadenoma invaded the cervix and produced multiple lung metastases, all of histologically benign type.

An ovary containing a pseudomucin cyst should never be resected. Apparently healthy portions may contain microscopic pseudomucinous glands (Fig. 270). On the other hand, if the second ovary appears normal, it should be left behind unless the patient has passed her climax.

It is unwise to puncture ovarian cysts in order to avoid large incisions. Such procedure increases the danger of wound implants and peritoneal dissemination. Rarely in huge cysts the danger of puncture is exceeded by the risk of incising from ensiform to symphysis.

Malignant changes may occur in parts of a pseudomucin cyst or in the peritoneal implants of such a cyst.

If large areas become carcinomatous they appear as more solid, whitish, brainlike regions. More often no changes are apparent to the naked eye.

The epithelium becomes multilayered and polymorphous. Hyperchromatic nuclei, irregularity in shape and size, vacuolation, fenestration are noticeable. Alveolar distribution of epithelial cells within the septa is common.

Serous Cyst Adenoma.—This variety of ovarian tumor is less frequent than the preceding. Pflaume (l. c. 73) found the serous variety in 22.8 per cent, though Schmidlechner (149), in a much larger material, noted only 8.33 per cent.

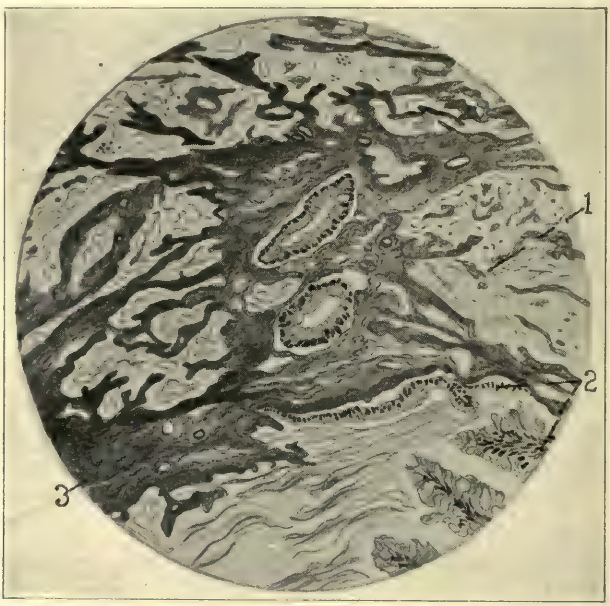

FIG. 269.—PSEUDOMYXOMA PERITONEI. (High power.) The jellylike pseudomucin is held together by honeycomb strands of new formed connective tissue (productive peritonitis). 1. Pseudomucin, debris. 2. Epithelial cells. In center of the field are two well-formed alveoli. 3. Connective tissue.

GROSS APPEARANCE.—Lobulation is less pronounced than in pseudomucin tumors, the cyst appearing unilocular, though usually small cysts are found in the wall of the main ones. The tumors rarely exceed the size of an adult head. They often are intraligamentous. The majority of serous cysts contain papillomata within the cyst. The fluid contents are thin, yellowish to brownish, or of greenish tinge, often turbid and flocculent but without mucoid or gelatinous elements.

Papillary excrescences were found by Pfannenstiel (l. c. 3, p. 162) on the surface of the ovary in 11 cases out of 100 tumors of the serous adenoma type, by Williams (150) in about 1 in 10, by Schmidlechner (l. c. 149) in 1 in 12.

Ordinarily the tumors are unilateral, but where papillary surface growths exist 60 per cent are bilateral and 50 per cent intraligamentous.

The surface papillomas may entirely substitute the ovary or may be pedunculated. The cauliflowerlike excrescences are soft, friable and vascular. In some, psammoma bodies may be present in such numbers as to produce a gritty feel. These tumors rarely grow larger than an adult fist.

Ascites regularly occurs when surface papillations are present. There may be papillae torn loose, floating free in the fluid.

Peritoneal implantations were found by Pfannenstiel in 13 per cent (l. c. 3, 1 : 343), by Martin (l. c. 4, p. 666) in 29 per cent. In Mansfeld's

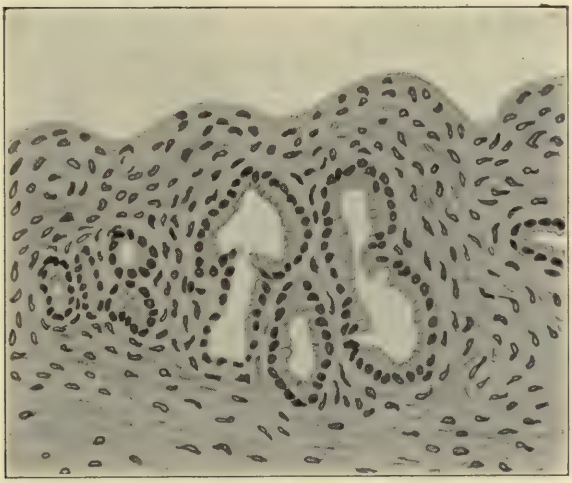

FIG. 270.—PSEUDOMUCIN GLANDS IN OVARIAN STROMA. (Medium power.) A small pseudomucin cyst was situated at some distance from the region of this section. This shows the inadvisability of "resecting" in case of pseudomucin cyst.

case (151) the implants invaded the substance of the uterus and the pararectal tissue. Usually they remain limited to the surface of the peritoneum.

Grapelike cyst adenomata are more common in the serous group. Pfannenstiel (l. c. 3, p. 170) was able to find 12, of which 4 appeared to come from ovarian rests on the posterior surface of the broad ligament. Frankl (l. c. 151a, p. 206) by 1914 found five additional cases (Jayle and Bender, 152).

The cysts may have long or short pedicles. Their walls are thin. The interior may be papillated. The inner lining is the typical low, cylindrical, ciliated epithelium (Fig. 271). Externally, low cuboidal or flat endothelium may be found, though it is often lacking.

The chemical composition of the fluid in serous cyst adenomata is that of dilute blood-serum. The albumin contents is high. There is no pseudomucin.

The microscopical appearance of the epithelium is similar whether a

smooth cyst wall, papillae inside the cyst (Fig. 272) or surface papillomata are examined.

As Gebhard (l. c. 38, p. 336) suggests, fresh scrapings of the epithelial lining should be examined in normal salt solution to demonstrate the cilia of the epithelium. This epithelium is low cylindrical and resembles that of the uterus in its granular protoplasm and centrally situated, darkly staining nucleus (Fig. 267E, p. 389). The cells are of uniform size and in one layer.

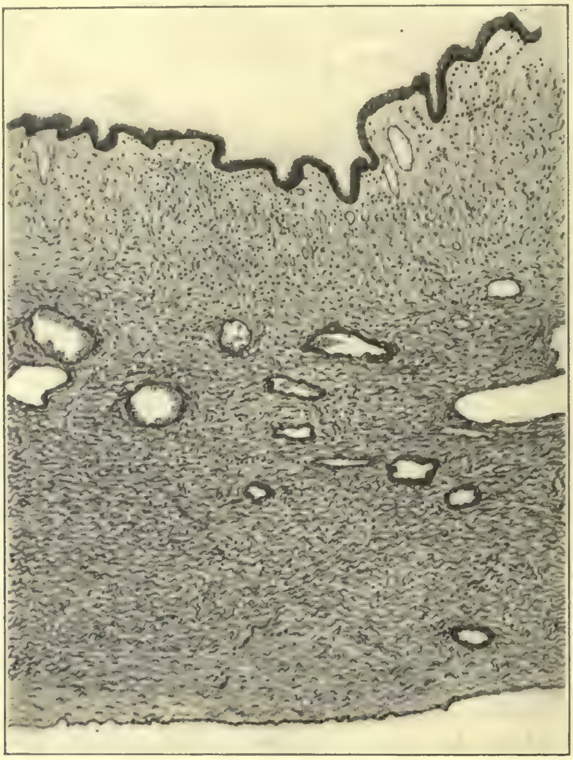

FIG. 271.—WALL OF A SEROUS CYST. (Medium power.) Above, the gland epithelium is dark staining and ciliated. The cyst wall is thick and vascular. The peritoneal endothelium is plainly shown below.

Glandular proliferations are regularly found in the septa and cyst walls. The framework of the papillae consists of soft, cellular connective tissue which, especially in the surface papillae, may be edematous, causing a resemblance to the "grapelike" papilloma (p. 382). In the latter the secreting epithelium is inside the cyst, in the former on the outside of the stroma.

Psammoma granules are often found in the epithelium and stroma. These granules do not denote either lack of vitality of the tissue or malignancy. Ewing (153) says that they are preceded by colloid degeneration.

RESULTS AND CURES.—Pfannenstiel (l. c. 3, p. 168) obtained 77 per cent of cures, Schmidlechner (l. c. 149) 82.5 per cent, and Pflaume (l. c. 73) 93.5 per cent. These tumors are a greater menace than pseudomucin cysts, but yet benign. Papillary forms are cured in only 50 per cent, according to Fromme (154).

As 60 per cent of the papillary forms are bilateral (although sometimes long intervals elapse before the second ovary shows tumor formation), the unaffected ovary should be removed prophylactically, except in very young patients.

FIG. 272.—PAPILLARY FORMATIONS INSIDE OF A SEROUS CYST ADENOMA. (Low power.) Markedly irregular and interdigitating papillae line part of the cyst. The epithelium, where it is cut perpendicularly, is in single layer.

Pfannenstiel (l. c. 3, p. 167) was able to find a dozen cases in the literature where peritoneal implantations appear to have regressed after removal of the primary ovarian growths. Flaischeln (155) describes such a case in which 22 years had elapsed since operation. Late recurrences are also on record (Olshausen, after 21 years, recurrences in the abdominal scar).

Incomplete operation is always followed by recurrence and death (Pfannenstiel, l. c. 3, p. 168, nine cases). Sometimes long periods of comparative well being intervene, as 18 years in Schroeder's case (l. c. 141).

Scar recurrences were discussed on p. 390. They are uncommon.

Carcinomatous changes occur in serous cyst adenomata. Sometimes

slow-growing papillary tumors suddenly take on malignant qualities, more often the new growth shows cancerous qualities early. Direct transitions from papillary serous cyst adenoma with a quiet single layer of epithelium to bizarre, polymorphous, multilayered epithelium, and typical adenocarcinomatous areas can be traced. (See Fig. 274, p. 400.)

Grossly, such tumors show solid areas in the cyst wall. These areas are pinkish to yellow, soft and friable. On section, "cancer juice" can be squeezed from the surface with the back of the knife. Papillae either fill the cyst lumen, grow diffusely on the outer surface, or both.

These growths are malignant but do not recur as readily as the solid cancers (Hoehne (156), of 34 cases of papillary cancer 16 died in two years, as compared with 25 non-papillary cancers of which 23 died; Pfannenstiel (l. c. 3, p. 139), 20 of 24, or 83.3 per cent).

3. CARCINOMA OF THE OVARY

Primary.—Frequency.—Primary cancer of the ovary is found in approximately 10 to 12 per cent of ovarian neoplasms (Lippert (l. c. 95), 10.66 per cent). Composite statistics of 1289 neoplasms showed 161 carcinomas, or 12.5 per cent.

If exact statistics covering cancerous pseudomucinous and serous cystadenomata were available, the percentage would doubtless be higher. These growths must be regarded as primary ovarian adenocarcinomata. Dermoid cyst supply a small contingent—according to Lippert (l. c. 95), 3 per cent; Wiener (l. c. 90), 3 in 60, or 5 per cent; Hoehne (l. c. 156), 3 in 55, or 5.4 per cent. Almost all are squamous-cell cancers from the epidermis of the dermoid. Solid cancers form the remainder of the group.

Site.—In 90 cases of Kelly's (l. c. 76, II, p. 305) 36.7 per cent were bilateral; Lippert (l. c. 95) found 46 per cent bilateral, Pfannenstiel (l. c. 3, p. 193) as high as 90.9 per cent, including cases in which cancer later developed in the remaining ovary. Very probably a number of metastatic growths are erroneously included.

Age.—Pfannenstiel (l. c. 3, p. 193) found the decade between 45 and 55 years most prone to cancer of the ovary. Papillary tumors occur earlier. Children are by no means exempt though doubtless many teratoid tumors are here included: Ahlfeld (157), congenital; Rosanoff (158), child of 5 years; Parry (159), 7 years; Lahey and Haythorn (160), 11 years; Meyer, R., l. c. 164), 10 years, etc.

Ascites is found in 78 per cent (Lippert, l. c. 95). It is often bloody, and, especially in the papillary types, tumor cells may be found in the centrifuged sediment. Intraligamentous tumors rarely cause ascites. In the late stages pleural exudates may develop.

Macroscopic Appearance.—Cancerous cyst adenomata, especially the papillary types, have been described on page 394 and page 397. Those arising from dermoids are dealt with on page 424.

The primary solid growths form small or medium sized, ovoid or round, often nodular tumors, which are firm and well encapsulated until the tumor tissue breaks through this envelop and spreads in mushroom form through the rent. Adhesions to neighboring viscera develop early. Depending upon the amount of fibrous tissue, the tumors are hard or soft. Pfannenstiel (l. c. 3, p. 178) emphasizes the shortness of the pedicle.

Kaufmann (l. c. 160*a*, p. 968) describes bilateral tumors weighing together 16 pounds.

On section the surface of medullary growths is found soft, brainlike, divided by septa of connective tissue. The color is reddish yellow, marbled by red and brown areas of hemorrhage. Necrotic parts have a baconlike

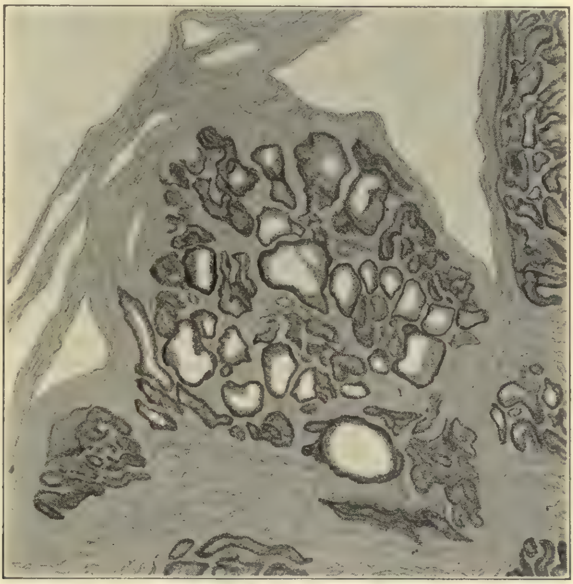

Fig. 273.—Adenocarcinoma of the ovary. (Low power.) Normal glandlike structures are closely imitated. The cells are of uniform size. Diffuse invasion of stroma is seen in spots.

sheen. Cysts due to liquefaction are numerous. Their walls are ragged; their contents may be grumous mush or cloudy fluid. These cysts are found near the surface. Scirrhous types of cancer resemble fibromata. Areas of calcification may be visible to the eye, or diffuse psammoma development may give a sandpaperlike feel to the tissue.

Microscopic Appearance.—As in other organs, transitions from adenomatous types, which in this case betray their origin from pseudomucinous or serous cyst adenomas occur. The cancerous areas are often solid.

Fig. 273 shows a rare form in which an adenomatous glandular type is preserved. There is little variation in the size of the cells and in that of their nuclei.

Fig. 274 shows the enormous proliferation of epithelium which occurred in a previously benign serous cyst adenoma which suddenly developed malignant qualities.

FIG. 274.—ADENOCARCINOMA DEVELOPING IN A SEROUS CYST ADENOMA. (Light power.) Papillary type with enormous epithelial proliferation. Below and to right a single layer of epithelium covers the papillae.

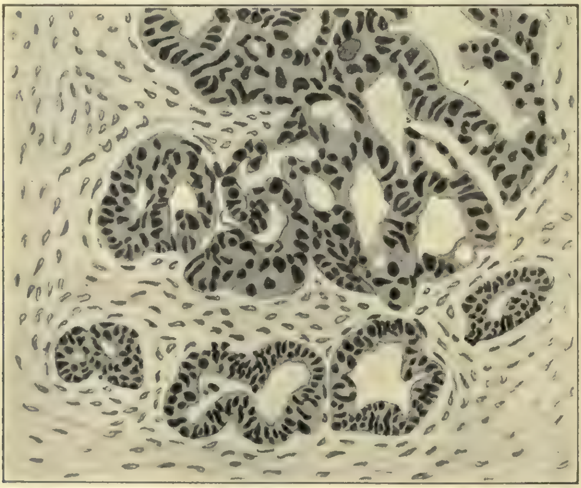

FIG. 275.—ADENOCARCINOMA OF THE OVARY. (Medium power.) All transitions from perfect alveoli to bizarre convolutions and solid portions were found in this growth. Origin from a pseudomucinous or serous group is no longer traceable.

Fig. 275 is taken from an adenocarcinoma (solid) which no longer can be referred to the pseudomucin or serous group. Polymorphism is marked.

Fig. 276, though derived from a cystic tumor, shows small cells resembling those seen in endothelioma. The arrangement is still adenomatous.

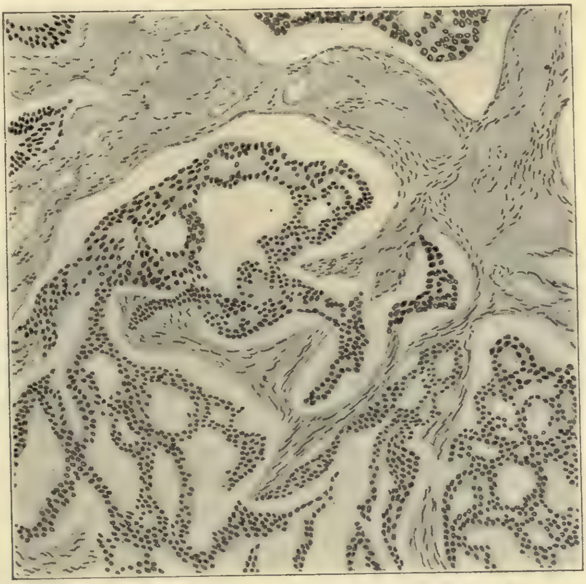

FIG. 276.—ADENOCARCINOMA OF THE OVARY. (Medium power.) A cursory resemblance to "adenoma malignum" of the uterus can be noted, but the cells appear almost like those of an endothelioma.

Fig. 277, although still adenomatous, approaches the solid type.

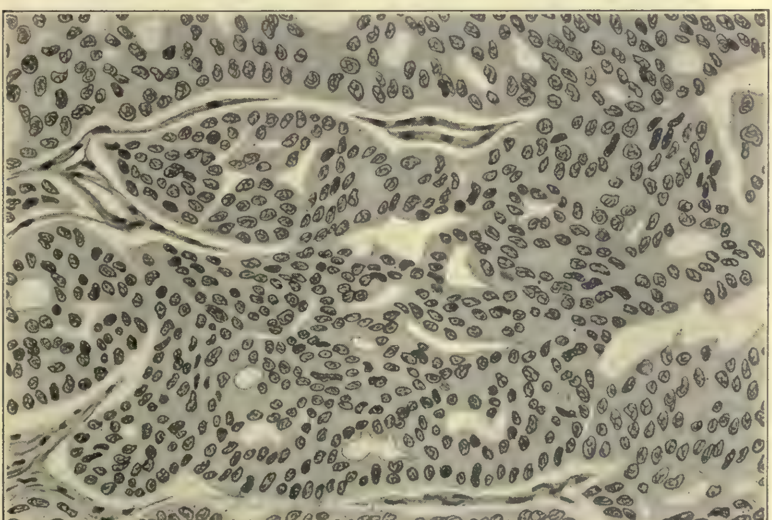

FIG. 277.—ADENOCARCINOMA OF THE OVARY. (Medium power.) This growth approaches the type of carcinoma solidum.

In Fig. 278 the transition to solid cancer is complete. It is an undifferentiated form.

Pfannenstiel (l. c. 3, p. 181) refers to the frequency of mucoid degeneration with resulting cyst formation. However, "colloid" cancers are most often secondary to gastro-intestinal growths (see p. 405).

In scirrhous forms the connective tissue preponderates. It may show myxomatous or hyaline changes.

Squamous epithelioma, except in dermoid cysts, is rare. v. Hansemann (161) and Lindermann (162) described cases.

FIG. 278.—CARCINOMA SOLIDUM OF THE OVARY. (Medium power.) This is an undifferentiated type of solid ovarian cancer.

Psammoma bodies are of frequent occurrence in the epithelium and stroma (Fig. 279). They do not signify malignancy, being also found in innocent growths.

To summarize; in ovarian cancer transitions from pseudomucin and serous types of epithelium can be traced throughout the adenocarcinomas. Many of these tumors are papillary. Gradually this origin disappears and with its disappearance the glandular formations are replaced by close packed, cohering papillae and solid alveoli, until finally medullary cancers are reached. In rare instances (vide ante) well-differentiated squamous epitheliomata have been described.

SPECIAL TYPES.—*"Folliculoma ovarii malignum," "carcinoma folliculoides,"* and *"granulosa cell" carcinoma.*—Under these appellations a number of solid tumors have been described which present:

(*a*) Folliclelike conglomeration of cells, containing vacuolations amid a

dense stroma (v. Kahlden (163) type). In some a thecalike mantle of cells surrounds the alvelous (Meyer, R., 164). If large degenerating cells are encountered in the vacuoles a striking resemblance to graafian follicles results. Hence Gottschalk, Hönnberg, Voigt (165) considered these growths ovogenic. On the other hand Liepmann (166), and Ingier (167), considered them as regressive metamorphoses.

(*b*) Cylindromatous tumors, with less connective tissue (Meyer, R., l. c. 164), the alveoli being larger. In spots labyrinthine convolutions consisting of long chains of single cells interweave in patterns resembling watered silk. (For literature see Meyer R., Monatschft. f. Gynäk 1916, 44).

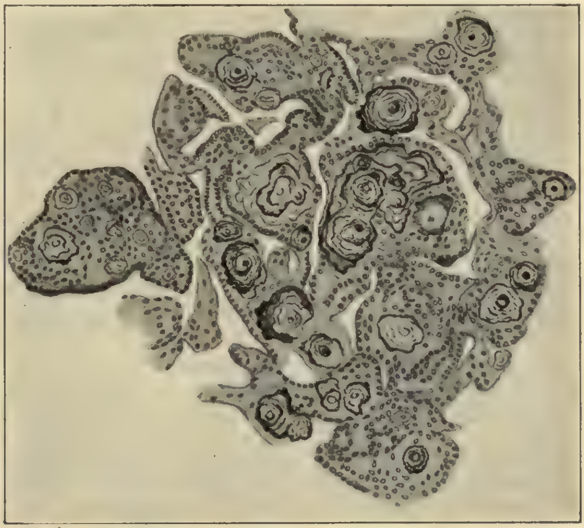

Fig. 279.—Psammocarcinoma of the ovary. (Medium power.) In a solid carcinoma with a tendency to pseudoalveolar formations, psammoma particles are seen. Concentric layers of calcification give a sandpaper-like feel. Decalcification, before sectioning is necessary.

The above tumors are derived from the granulosa cells by Meyer. Struma ovarii (see p. 420) has been confounded with this group.

Cancer of the ovary in hermaphrodites and in congenital anomalies.—Meyer (l. c. 164) here places the case of Keller in a female pseudohermaphrodite and four cases of his own where the genitals were aplastic; also two cases in male pseudohermaphrodites (Zacharias, Zucker, l. c. 164).

According to Meyer the main characteristics are the very loose relations of the epithelial cells, which are widely separated and without connective tissue support. The cells are 15μ in size, mitoses are few. Pick declares his chorion ectodermal tumor of the ovary (Langhans' cell type) identical with these tumors (Fig. 294, p. 427).

The writer believed that all these tumors are teratoid and sometimes approach the alveolar sarcoma, sometimes the carcinoma in type.

Metastases and Extension.—No statistics are available. Peritoneal implantations are the most frequent. The pelvic peritoneum is first involved, later the entire abdomen may be affected. Diffuse peritoneal carcinosis results. Omental metastases are the most bulky. The serosa of every abdominal organ may be affected. The implants are morphologically identical with the primary growth. They invade the subperitoneal tissues and the parenchyma of organs.

Invasion by continuous growth involves the broad ligaments, tubes and uterus. Later the entire pelvis becomes converted into a carcinomatous mass.

The lumbar glands are regularly affected. Gebhard (168) found the inguinal glands involved. Supraclavicular metastases were noted by Villard and Murad (169).

Werner (170) in ten cases of coincident cancer of the uterus and adnexa found 6 primary in the ovary. In the 4 primarily uterine the tubes but not the ovaries, were involved. Of the above 6 cases 2 spread by continuity and 4 metastasized (2 serous, 1 muscle, 1 mucosa of the uterus).

The liver may show metastases, the lungs also. So-called metastases in the gastro-intestinal tract and breast are most often misinterpretations, the primary growth being situated in these organs (see secondary ovarian cancers, below).

Cures and Results.—Pfannenstiel (l. c. 3, p. 245) found recurrences in 83 per cent of papillary and in 66 per cent of solid cancers. The cures effected by others were even fewer. While unilateral cancers recurred in 43 to 50 per cent, bilateral showed 89.5 and 90 per cent (Fromme, l. c. 154, Hofmeier, 171). Absolute cures according to Winter's formula (see carcinoma cervicis) were only 14.64 per cent.

Döderlein (172), in 82 cases of ovarian carcinoma, found 7 so far advanced that even exploratory incision was contra-indicated, in 11 only exploratory incision was done, in 46 incomplete operations were performed (metastases, etc.), while in only 18 could radical removal be practiced.

In cancer of the ovaries a panhysterectomy should be performed. Pfannenstiel advises against removal of the lymph glands, as he says that if the accessible ones are involved, the inaccessible ones are invariably affected.

Cancer may develop in the ovarian portion of a tubo-ovarian cyst (see p. 336).

Secondary (*Metastatic*) Frequency.—Secondary ovarian growths are frequent. Many cases of so-called bilateral primary growths would doubtless, on autopsy, prove to be secondary to unrecognized gastro-intestinal or mammary cancer.

Schlagenhaufer (173), in 79 cases of ovarian cancer with the primary growth in the abdominal viscera, found the origin as follows: 61 gastric,

10 intestinal, 7 gall bladder, 1 pancreas (?); Döderlein (l. c. 172, p. 695) in 80 ovarian cancers, found the stomach involved in 13. Handley (174), in 422 autopsies of mammary cancer, found metastases in the ovaries in 4.8 per cent of "early" cases and in 8.6 per cent of "late" ones; Torek and Wittelshoefer (175) in 7 per cent. The uterus (Werner, l. c. 170), Taussig (176) is the organ primarily involved in a small number of cases, metastases from cervical cancer being less frequent than from corporeal growths. The tube is occasionally the primary site (see tubal cancer, p. 353).

Route.—The routes by which the ovaries are reached by cancer cells from different organs are various. Direct extension, peritoneal implantations, lymphatic transportation by way of the retroperitoneal and the superficial lymphatics and dissemination by the blood stream may singly or together play a rôle.

In uterine and tubal cancer invasion by direct extension may take place.

In gastro-intestinal cancer, after the serosa has been perforated, minute implants collect in Douglas' cul-de-sac and gain access to the ovary through the rupture in the follicle wall at the time of menstruation or through the intact germinal epithelium at any time (Glockner, 177).

Lymphatic infection may take place via the retroperitoneal lymph channels and, retrograde, through the spermatic chain to the hilus of the ovary (Glockner, l. c. 177; Roemer, 178).

In breast cancer Handley (l. c. 174) believed that cancer spread along the deep lymphatics of the abdominal wall and by means of the epigastric triangle, entered the abdomen. Glockner (l. c. 177) considered embolic transportation by blood channels of importance. At times the liver and retroperitoneal lymph nodes form the intermediate depots. For literature see Stone (179).

Macroscopic Appearance.—In the early stages small nodules may be found on the surface or in the substance of the ovary. Ordinarily, bilateral (in over 50 per cent) nodular tumors enlarging the ovaries to the size of an adult fist are encountered. The shape of the ovary may be preserved. A well-marked capsule is present. The ovarian tumors may in turn form the starting point of further extension (uterus, tube, retroperitoneal lymphatics (Schenk and Sitzenfrey, 180). Frankl (l. c. 151a, p. 212) describes a tumor the size of two pregnant uteri when at term. Such dimensions are exceptional. The color of the growths is grayish yellow, the consistence hard. Section shows an edematous, semi-transparent or waxy tissue, especially in growths originating from the gastro-intestinal tract.

Microscopic Appearance.—The typical Krukenberg tumor (181) which was first classified as a "fibrosarcoma mucocellulare carcinomatodes" and believed to be a primary ovarian growth, shows a sarcomalike edematous connective tissue. This is composed of spindle cells and of connective tissue cells of various size, shape and staining quality, with

edematous, myxomatous and necrotic areas. Amid this background are epithelial cells producing mucus. The cells may be empty or so filled that the nucleus is pressed against the cell membrane in crescent form, the so-called "seal-ring" cell. The cells are scattered in the stroma (Fig. 280) or together may form typical alveoli (Fig. 281).

It is conceivable that Krukenberg tumors may be primary. A careful autopsy alone can substantiate such a claim. Sternberg (182) and Glockner (183) appear to have described such cases. There may be others, but a minute examination of the gastro-intestinal tract is necessary. For literature see Major (184).

Metastases resemble the primary growth. From the uterus adenocarcinoma, squamous-cell cancer (Taussig, l. c. 176), from the breast scirrhus are most frequent.

For the sake of completeness, cancer metastasizing into an ovarian cyst should be mentioned.

Borrmann (185) describes a squamous cervical cancer producing multiple foci in a cyst, Forssner (186) a tumor originating in the intestine.

FIBROMA; FIBROMYOMA

Fibroma.—These growths are hard, usually diffuse growths which retain the shape of the ovary until they attain large size. They may have a kidney-like retracted hilus.

Frequency.—Höhne (l. c. 156) found ovarian fibromata in 1.3 per cent of 221 ovarian tumors, Pflaume (l. c. 73) in 1.4 per cent, Kelly (l. c. 76, II, u. 273) 5.9 per cent in 555.

Age.—*Peterson* (187), in 83 cases, found the ages as follows:

Years	No.	Per cent
10 to 20 years	7	8.43
20 to 30 years	20	20.09
30 to 40 years	16	19.27
40 to 50 years	23	27.71
50 to 60 years	11	13.25
60 to 70 years	5	6.02
70 to 80 years	1	1.20

Ascites is present in all cases, unless the growth is minute. In addition, the patient may show a distinctly cachectic appearance.

Bilateral growths occur in 20 per cent.

Adhesions were present in 26 per cent of Peterson's cases (l. c. 187).

Macroscopic Appearance.—In circumscribed tumors, small, often superficial and pedunculated nodules of white to pinkish, pearly appearance are found embedded in the ovary, without capsule formation.

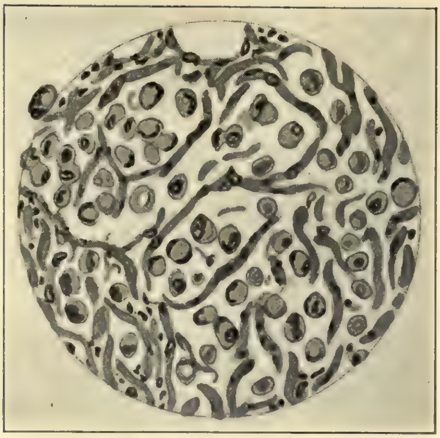

FIG. 280.—KRUKENBERG TUMOR: METASTATIC OVARIAN CARCINOMA. (High power.) Secondary to gastro-intestinal cancer. "Sealring" cells due to accumulation of mucus intracellularly lie in a sarcomalike connective tissue.

FIG. 281.—METASTATIC OVARIAN CARCINOMA. (High power.) Secondary to an intestinal growth. To the right are "seal-ring" formation, to the left true alveoli.

Diffuse growths entirely replace the ovarian stroma or originating from one pole, leave an ovarian rest. They may be bony hard, or cartilaginous or of the consistence of a soft uterine myoma. A thin fibrous capsule encloses them. The surface is often nodular. The color may be white and tendinous, or gray to pink. When torsion of the pedicle has taken place (see p. 384) the color becomes bluish or black. Thin-walled veins may course over the tumor.

Clemens (quoted by Pfannenstiel, l. c. 3, p. 308) described a fibroma weighing 40 kg., Jacoby (188) one of 30 kg., Titus (189) one of 35 pounds.

Fibromata may occur in the wall of ovarian cysts. Pfannenstiel (l. c. 3, p. 314) describes the small pedunculated growths found on the surface of the ovary as a separate variety (fibroma papillare ovarii).

Rokitansky classed large corpora fibrosa as fibromata.

Necrosis with secondary liquefaction is common in fibromata. Cysts may be due to dilated lymph vessels.

Calcifications take place in necrotic areas (Williams, 190). This author mentions a case of Spencer Wells which attained the size of a coconut and had to be cut with a saw. Usually the calcified areas are small.

"White stones" composed of magnesium and calcium phosphate and carbonate, found loose in the ovarian stroma, most often arise from a corpus luteum (Ries, 191). They can be readily shelled out. They may contain a cavity.

Ossification is likewise known. It occurs in calcified areas. Such areas were previously described as osteomata. They most often occur in corpora lutea or albicantia. In Buet's case (192) the bony portions of the tumor were the most conspicuous portions of the large growth.

Microscopic Appearance.—Fibromata are composed of connective tissue cells amid a fibrillar stroma (Fig. 282). Bundles cross each other without regularity, but an histologically quiet picture results. This distinguishes fibroma from sarcoma in which closely packed cells and nuclei varying in size and chromatin content appear (Fig. 284, p. 412).

Edema separates the connective tissue cells and, when it persists, these cells may assume star shapes. It is questionable whether the myxomatous changes reported are true myxomatous degeneration or edema (Kroemer, l. c. 3, Veit, p. 320). Myxoma is found as part of sarcoma.

Necrosis causes disappearance of cell outlines and nuclear markings until all details are lost in the remaining detritus.

Calcification shows as small discrete deposits or diffuse, deeply staining areas. Coe (193) showed lutein cells around the calcified areas. In ossification, bone lamellae with Haversian canals, marrow and osteoblasts may be found. Moschcowitz (194) (Fig. 283). Such findings must be differentiated from bone in a dermoid or teratoma (Robertson, 195). For literature see Outerbridge (196).

Chondroma appears only as a constituent of a chondrosarcoma (see p. 414).

For literature see Coe (193), Williams (190), Peterson (187), Hellmann (197).

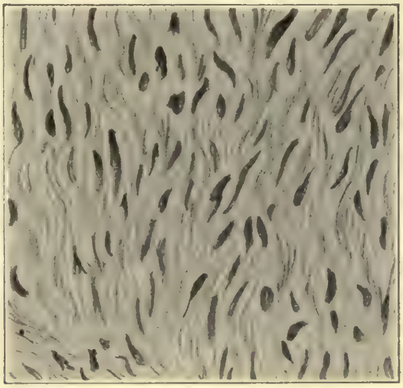

FIG. 282.—FIBROMA OF THE OVARY. (High power.) Nuclei are scattered in fine fibrillar tissue. The nuclei do not vary in size. Mitoses are absent.

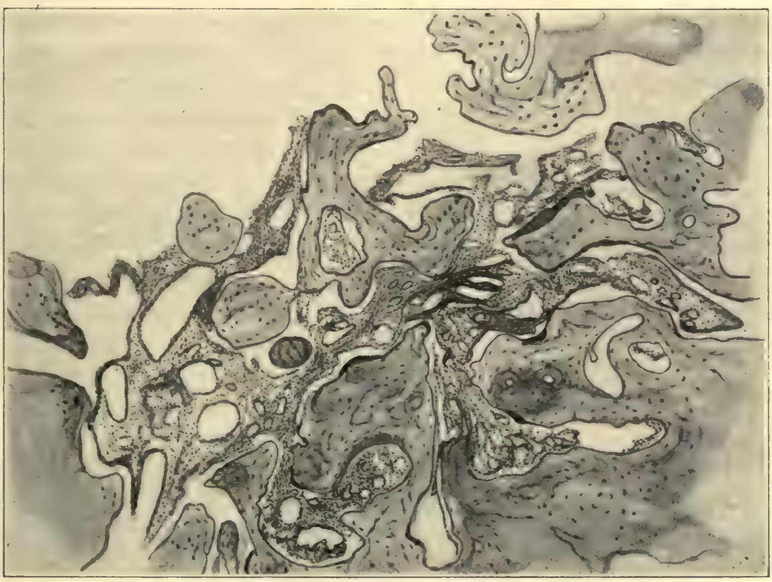

FIG. 283.—OSSIFICATION IN THE OVARY. (Medium power.) Bone with Haversian canals was found embedded in the ovary. Between the bone is fatty marrow. (Case of Dr. Eli Moschcowitz.)

Fibromyomata.—Fibromyomata contain various amounts of unstriped muscle tissue in addition to fibrous tissue. The muscle may preponderate. Like the fibromata, they are not encapsulated.

Kroemer (l. c. 3, p. 318), of 69 fibroid tumors, found that only 17 were fibromyomata. Basso (198) has collected 45 cases. These leiomyomata undergo the same degeneration as do the fibromata.

Frankl (199) describes a huge fibromyoma.

Hartz (200) reports sarcomatous changes in a fibromyoma (round-celled sarcoma).

Results.—All authors are agreed that 100 per cent of cures are obtained by removal of the growth.

Adler (201) describes an *adeno fibroma intracanaliculare.* The ovary was double the normal size, fibrous in consistence and traversed by minute clefts in every direction. These clefts were lined with ciliated cylindrical epithelium. He derives the tumor from the epoöphoron (?).

ANGIOMA OF THE OVARY

Hemangioma.—This is a very rare and unimportant tumor. Some of the so-called hemangiomata were agglomerations of hilus vessels in chronically congested ovaries, or varices of the utero-ovarian venous plexus (case of Kroemer, l. c. 3, p. 332). Marckwald (202) found a small (hazel-nut size) tumor at autopsy. Orth (203) in a child with multiple hemangiomata (skin, internal organs) describes both ovaries involved.

Lymphangioma.—Kroemer (l. c. 3, p. 333) describes a tumor twice the size of a child's head, firm, whitish. The mass on section proved polycystic, the septa porous and thin. A thin serous fluid oozed from the tissues. At the periphery typical angiomatous formation was found (see angioma of vulva, Fig. 93, p. 116). In another case a small angiomatous area was found in which the endothelium and stroma formed cell mantels around the lumina.

For lymph angioma in a teratoma see p. 424.

SARCOMA OF THE OVARY

Primary Sarcoma—Frequency.—Sarcomata form from 2 to 5 per cent of ovarian growths: Pflaume (l. c. 73) 2.1 per cent, Lippert (l. c. 95) 2.5 per cent, Kelly (l. c. 76, p. 273) 2.7 per cent, Fromme (l. c. 154) 3.1 per cent, Pfannenstiel (l. c. 3, p. 340) 5.4 per cent.

Age.—The average age, according to Temesvary (quoted by Kroemer, l. c. 3, p. 383), is 32 years. Pfannenstiel (l. c. 3, p. 383) says that 40 per cent are under 25 years. Doran (l. c. 77) discovered bilateral round-cell sarcoma in a seven-month fetus. Hubert (204) was able to collect 200 ovarian sarcomata in children. In the writer's experience ovarian sarcoma has, in the majority of cases, occurred in individuals between 18 and 25 years.

Statistics are unreliable, as many of the older authors include Krukenberg tumors (see p. 404) among the primary sarcomata. Of 130 cases collected by Stauder (205) 42, or 32.3 per cent were bilateral. Ascites, often bloody, is present in a majority of cases, 60 to 70 per cent.

Macroscopic Appearance.—The majority are solid tumors, hard if of the fibro-sarcomatous type, softer as the connective tissue elements decrease. Round-celled sarcomata are soft, friable and resemble brainlike tissue; spindle-cell tumors are whiter and firmer. The surface is smooth or slightly nodular, the color reddish white or yellow. The shape of the ovary is often retained and the hilus may be retracted as that of the kidney. Adhesions are frequent.

On section hemorrhagic, necrotic (dry yellowish) or liquefied areas produce a marbled surface. Lymphatic dilations appear as small, smooth cavities.

Rarely sarcoma develops in the wall of a preformed cyst (Cullen, Taylor, 206).

The tumors may be so soft that they rupture during examination, Kelly (l. c. 76, II, p. 323) thus almost lost a patient from internal hemorrhage. The tumor may tear and disintegrate during removal, thereby increasing the risk of recurrence.

Microscopic Appearance.—According to the predominating cell types sarcomata are divided into unripe and ripe forms. The unripe types (round-cell, polymorphous and giant-cell, and myxosarcomata) approach most nearly to the embryonal types. The spindle-cell, muscle-cell (myo), chondro- and osteosarcomata contain well differentiated cell types. Usually combination forms are found, as spindle with round-cell, etc.

Among the 100 cases he collected, Wolff (207) found the following varieties:

Spindle-cell	44	Melano (primary)	3
Round-cell	38	Myxo	2
Mixed cell	5	Osteo	1
Fibromyxo	4	Questionable	3

In addition to the nomenclature based on the cell variety, further description is based upon the relation to blood vessels (s. hemangiectaticum, s. perivasculare) and lymph vessels (s. lymphangiectaticum). Often both designations are combined.

The spindle-cell sarcoma (s. fusicellulare) is a firm, slow growing tumor of whitish color. It is distinguished from a fibroma by the less differentiated fibrillar structure, the great differences in the size and tinctorial qualities of the nuclei, the plumpness of the cells and the general impression of unrest (Fig. 284).

There may be multinuclear cells or round cells in areas of the tumor. Perivascular distribution, telengiectatic areas or cystic portions are not

uncommon. Areas of necrosis, with preservation of the neoplastic tissues around the vessels or close to the main septa are found.

Round-cell sarcomata (sarcoma globicellulare) may be further subdivided into small, and large round-cell, and alveolar round-cell types. They form the soft, encephaloid, rapidly growing tumors encountered in the youthful and contain hemorrhagic, necrotic and liquefying areas with many small cystic spaces.

Wolff (l. c. 207), in 18 round-cell sarcomata, found 1 large, 9 small and 8 alveolar sarcomata.

Fig. 285 shows a large round-cell sarcoma of unusual type removed from a girl 12 years old. The cells are grouped in long columns with an occasional lighter and larger central cell.

FIG. 284.—FIBROSARCOMA OF THE OVARY. (Medium power.) Nuclei of varying size and tinctorial qualities in a fine stroma. The section resembles a uterine myosarcoma.

Fig. 286 shows a small round-cell sarcoma of perivascular distribution. The degenerated connective tissue becomes unduly prominent because innumerable cells have fallen out of the section.

Fig. 287 shows a large-celled alveolar sarcoma.

According to Wolff (l. c. 207) the tumor thrombi found in the veins contain no connective tissue. He therefore regards the septa in alveolar types as derived from the organ in which the sarcoma grows.

These growths are often glycogenic and may show numerous mitoses. Hartz (l. c. 200) describes a fibroma (6.2 kg.) with sarcomatous changes (round cell) and has collected two other cases from the literature. Kroemer (l. c. 3, p. 389) reported a sarcomatous area in a serous cyst adenoma which one year later recurred in the cervix and caused death.

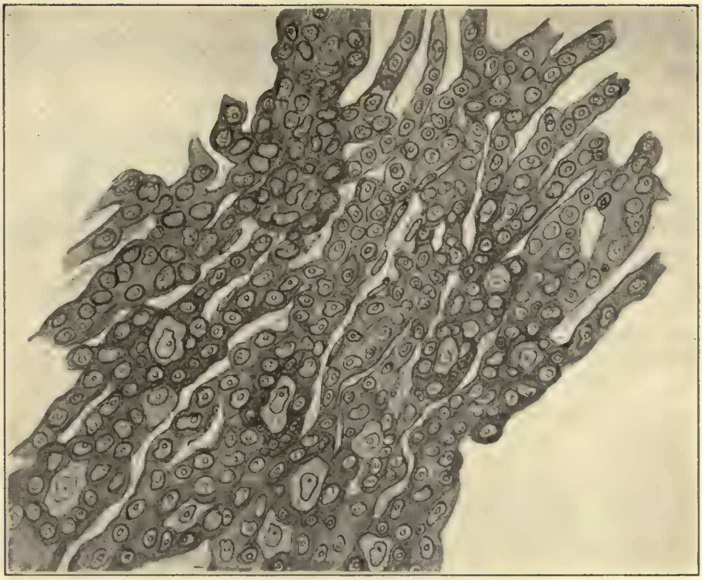

FIG. 285.—LARGE ROUND-CELL SARCOMA. (Medium power.) Grouped in columns with occasional lighter cells.

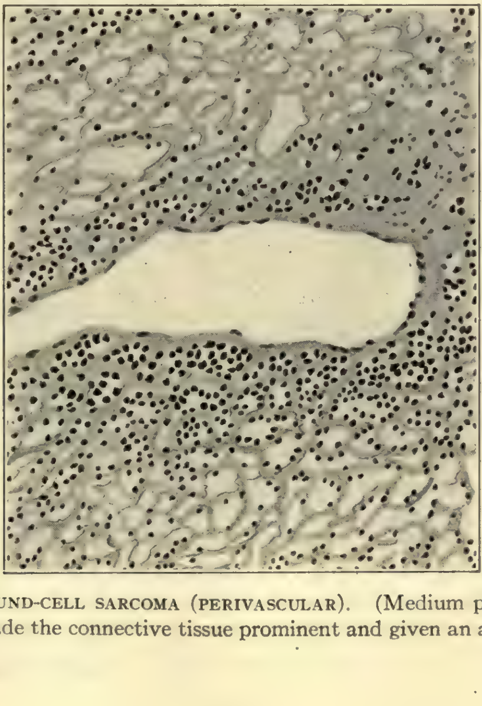

FIG. 286.—SMALL ROUND-CELL SARCOMA (PERIVASCULAR). (Medium power.) Degeneration and swelling has made the connective tissue prominent and given an alveolar appearance.

Polymorphous or mixed-cell sarcomata are recognized by the marked differences in size and shape of the cells. Giant cells are of frequent occurrence. These tumors usually show regressive changes.

Fig. 288 shows a tumor with so-called parenchyma giant cells (large polygonal nucleus, large body). In Fig. 289 the giant cells are of the foreign body type, amid smaller variegated cells and a fibrillar intercellular substance.

Myxosarcoma is commonly found in areas of any of the previously described varieties. Star cells with two and three dendritic processes in a diffusely staining tissue are noted.

Myosarcoma appears in areas resembling leiomyoma in tumors composed of spindle or round cells. The unstriped muscle cells are like those seen in myosarcoma uteri (Fig. 166, p. 248).

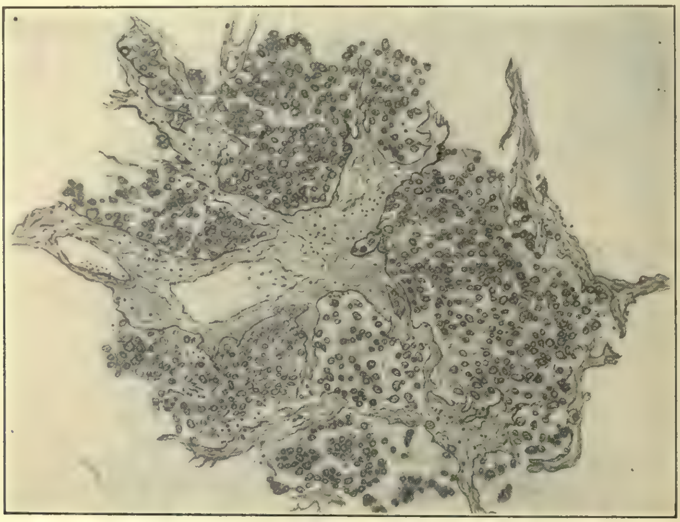

FIG. 287.—LARGE-CELLED ALVEOLAR SARCOMA. (High power.)

Chondro- and osteo-sarcomata, if not part of a teratomatous growth, signify further differentiation from an indifferent multipotential mesodermal anlage. The cases of Gibb (208) and Hammond (209) (myxochondrosarcoma) and Jung (210) (chondrosarcoma of the ovary and lymphendothelioma of the cervix with metastases arising from both) are examples.

Melanosarcomata are almost invariably secondary. The case of Andrews (211), where at operation, in addition to the black ovarian tumors, metastases existed only in the omentum and on the surface of the uterus, may have been primary. Amann (212) and Lorraine (213) found melanosarcomata arising from dermoid cysts. These are certainly primarily ovarian in origin (from the skin or choroid of the dermoids).

Bab (214) collected 36 cases in the genital tract, but they must be considered secondary. As the primary and secondary tumors do not differ greatly the two will be discussed together.

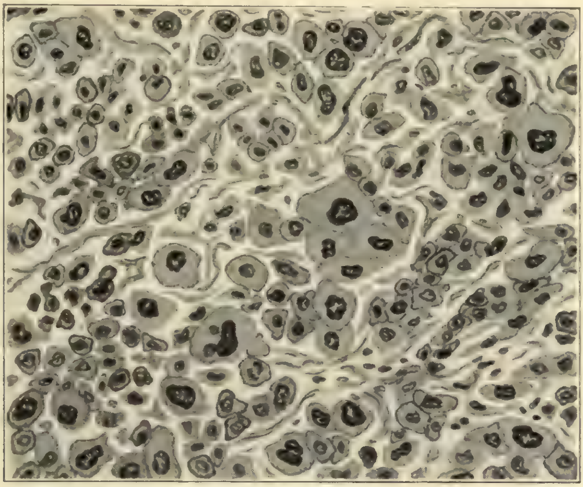

FIG. 288.—LARGE-CELLED POLYMORPHOUS SARCOMA OF THE OVARY. (High power.) The giant cells are of the parenchymal type.

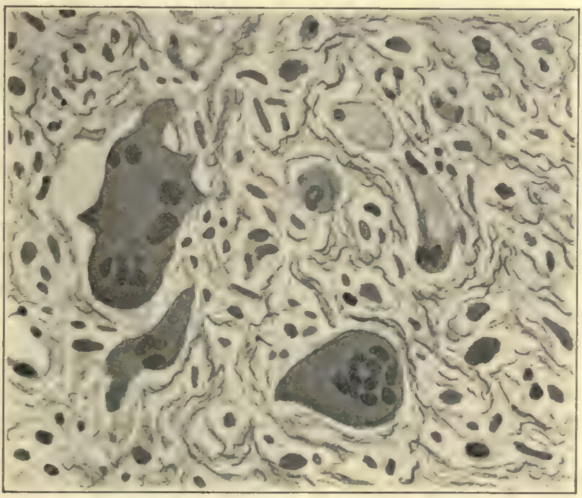

FIG. 289.—GIANT-CELLED FIBROSARCOMA OF THE OVARY. (High power.) The giant cells are of the foreign body type. The stroma is markedly fibrous.

The ovaries are changed into solid nodular, or partly cystic tumors of black or brownish color. In some cases readily shelled-out, black nodules are found in the stroma. Almost invariably numerous metastases occur throughout the abdomen.

The origin is in the choroid of the eye, pigmented skin tumors or the adrenal gland.

The growths consist of two components, the sarcoma cells (polymorphous or round-celled sarcoma) and the pigment carriers or "chromatophores."

The chromatophores are elongated, branching cells. Around the nucleus are coarse granules of the brown pigment *melanin* (Lubarsch, 215). Often the pigment is found in extracellular locations (see Fig. 104, p. 127).

The writer recalls an unpublished case of Hodenpyle's, in which six months after removal of an insignificant pigmented umbilical nevus, death occurred. Multiple metastases were found, most massive in the liver and ovaries. Only after considerable search and inquiry was a report of the ablation of the nevus obtained, because this insignificant occurrence had escaped the memory of the relatives.

RESULTS AND CURES.—Fibrosarcomata almost never recur. The prognosis becomes progressively worse as softer tumors have to be dealt with. Large alveolar sarcomata are the most malignant. Pfannenstiel (l. c. 3, p. 249) found 33 per cent of cures, which is far superior to the results obtained in carcinoma. Recurrence, when it takes place, is usually within 1 to 2 years.

Even bilateral tumors, if not metastatic, are curable (Pfannenstiel, 4 out of 14). In hard tumors simple removal, in softer growths bilateral oöphorectomy and supravaginal hysterectomy is advised.

Metastases may occur in all the abdominal organs. The uterus, tubes, stomach, liver, intestine, lungs, diaphragm, subcutaneous tissues are the most frequent sites.

Secondary Sarcoma.—*Melanosarcomata* (see p. 414) are almost invariably secondary. They metastasize by the blood stream.

Uterine sarcoma by direct extension, by lymphatic involvement or by perforating the serosa and discontinuous implantation, produces ovarian metastases. At times the pelvis is found to be occupied by a solid mass of sarcoma tissue involving all the internal genital organs. The point of origin is then no longer determinable.

ENDOTHELIOMA OF THE OVARY

Polano (216) was unable to demonstrate primary lymph spaces or perithelial spaces around the blood vessels. He showed in a number of instances (217) how adenocarcinoma and sarcoma are mistaken for endothelioma. Robert Meyer (136) denies their existence. The literature is collected by Barrett (218).

The tumors are supposedly 1. Lymphangio endothelioma intravasculare; 2. hemangio endothelioma intravasculare and 3. hemangio endothelioma perivasculare.

Their morphology (see p. 256, Uterine Endothelioma) shows alveolar, columnar or glandular arrangement (Pick, 219) and transition forms.

The so-called angioplastic sarcomata with chorionepithelioma-like areas and metastases (see Kroemer, l. c. 3, p. 375) are rubricated in this group if no teratomatous parts can be demonstrated.

The writer has modified his views concerning these and similar tumors (see p. 426) and regards the syncytial changes as explainable by functional response of cells to intimate relations with the blood. In other terms, when cells line blood channels they assume syncytial form. Therefore syncytial complexes need not be regarded as clinching the histogenesis. It is also known that degenerative processes may simulate syncytium by obliterating cell boundaries (symplasma). On the other hand, when good reason exists for considering these tumors as part of a teratoma, the morphology is as good a criterion of chorionepithelium as it is of brain substance, the choroid of the eye, or other tissues.

The "endothelial" tumors resemble sarcomata and undergo the same degenerations. According to Apelt (220) 22 per cent are bilateral. Ascites is regularly present. The mortality, according to Barrett (l. c. 218), is 37 per cent, but statistics are most incomplete. Kroemer (l. c. 3, p. 385) places the deaths at 57 per cent.

TERATOMA OF THE OVARY

These growths contain derivatives of the three layers of the embryo arranged in a more or less orderly fashion in dermoid cysts, and scrambled together in a "potpourri" in the solid teratomas. Their relation to each other from the clinical point of view resembles that of a benign adenoma to a carcinoma (Pfannenstiel, l. c. 3, p. 382). Bonnet (221) claims that an almost unbroken line can be traced from the acardiacus amorphus to teratomata in which atypical proliferation of some one constituent has overgrown the other constituents and thus produced apparently simple tumors.

Dermoid cysts will be discussed separately from solid teratomata, although the transitions from one group to the other are fluid.

Dermoid Cysts.—These cystic tumors externally resemble other unilocular cystic growths of the ovary to such a degree that they are often not recognized until the cyst cavity is opened and sebum and hair discovered.

Frequency.—They form from 5 to 25 per cent of all ovarian tumors, Olshausen (quoted by Gebhard, l. c. 38, p. 366) found 4 per cent in 2275 ovarian tumors. Pfannenstiel (l. c. 3) 10 per cent, Lippert (l. c. 95) 10.3 per cent, Kelly (l. c. 76) 16.2 per cent, Wiener (l. c. 90) 25 per cent.

Age.—Age incidence is not characteristic. The average age in Kelly's series (l. c. 76, II, p. 309) of 90 cases was 35 years. These cysts are found in childhood and in advanced old age.

Bilateral dermoids occur according to Gebhard (l. c. p. 366) in 15 per cent, to Pfannenstiel in 10 per cent of cases. Kelly in 87 found only one bilateral, and Wiener found one in 60.

Multiplicity.—At times multiple dermoids are encountered. Heinsius (*222*) found five dermoid plugs in one ovary. More often the dermoid anlage is partially cleft or split up.

Clinical Characteristics.—On page 385 the frequency with which dermoid cysts are subject to torsion of the pedicle, infection and rupture has been emphasized. Parasitic dermoids have also been referred to (p. 387). Dermoids have formed in a supernumerary ovary (Kroemer, l. c. 3, p. 215). In 5 of 12 cases dermoid cysts were found lying anterior to the uterus.

The diagnosis of dermoid cysts has been made by aid of the X-ray when bone and teeth were shown to be present (Wilms, 223). In case of rupture into the intestine or bladder the passage of hair or teeth has proved of diagnostic value. Perforation into the uterus can occur (Söderberg, 224). Such rupture is not due to malignant erosion but to atrophy of intervening septa by pressure or by inflammatory perforation.

Macroscopic Appearance.—Dermoid cysts are usually globular, smooth growths of dull white or bluish color. They are of moderate size, though Kelly removed one containing 10 liters of fluid. Often some portion of the ovary can be recognized as a flattened boss on the cyst wall. The cyst may be retroperitoneal or intraligamentous in a small proportion of cases.

On palpation of the unopened cyst, hard bony portions or teeth may be felt. As the cyst cools from body to room temperature a doughy consistence becomes noticeable. This is due to the hardening of the fatty contents.

Dermoid cysts may grow in close apposition to, or be incorporated in a pseudomucin cyst. The conjunction of these two varieties of cysts is too frequent to be considered a mere coincidence. Ribbert (l. c. 119) believed pseudomucin cysts are the entodermal portion of a dermoid anlage (see page 387). Norris (225) describes a dermoid complicated by an 80-pound cyst.

On the other hand, conjunction with lutein cysts, or follicle cysts which are quasi normal and constant constituents of the ovary must be regarded as accidental.

In consequence of this juxtaposition the interior of a dermoid cyst may show lobulation (remains of septa) or may be multilocular.

The contents consist of a fatty, yellow, butterlike mass, semi-solid at room temperature.

The mass is composed of fat (needles), detritus, epidermis cells, cholesterin crystals (Fig. 266).

Rarely the fat clumps in the form of balls which may reach the dimensions of a hen's egg, or form innumerable, small, ricelike bodies. The process has been compared to butter formation. It can result when a non-

miscible liquid such as serum enters the cyst and "breaks" the emulsion. This occurs after torsion of the pedicle (Plenz, 226). Gebhard (l. c. 38, p. 369) found balls twice in 107 dermoids.

The cyst contents rarely calcifies in the form of a stone. The cyst wall is thin and fibrous, rarely it is thick and may contain calcified, platelike spots. In one area, however, a thick nodular plug or projection ("Hoecker") projects into the cyst cavity. The cyst wall is lined with cuboidal or cylindrical epithelium, rarely with a low squamous layer.

The dermoid plug, which represents the embryonal anlage, is an elevation covered with white skin from which arises hair. At the edges of the plug the skin may end abruptly, being replaced by a glistening cyst lining, or the skin may gradually thin out, or islands of epidermis may be found scattered in different parts of the cyst.

The plug, in some instances, instead of merely projecting into the cavity, extends to the opposite wall, thus having a bipolar origin.

On inspection of gross sections, or with very low magnification, of the plug, a certain uniformity of arrangement will become apparent. The skin region corresponds to the scalp. Below this, within a fibrous capsule, often reinforced by bone plates, is the brain (pigmented area for eye anlage). In close conjunction are found bone masses with teeth.

Small openings entering the plug and a change to pinker mucosa often document the presence of entodermal constituents (respiratory and intestinal tracts). These are usually very rudimentary.

Thyroid tissue, bone, cartilage, subcutaneous fat may be recognizable. The above description is applicable to the great majority of dermoid cysts. However, far more *fetuslike tumors* have been described and also far less complicated growths.

Maydl (227), in a young man, found between the leaves of the mesentery, enclosed in an amniotic sac, a fetus with well-developed trunk and extremities. There was no head, but hair 50 cm. long. The cyst cavity was filled with oily fluid.

Shattock (228) reported an ovarian dermoid containing poorly developed lower limbs, a vulva and pubic hair, spinal column, also a blind coil of intestine in a coelomic cavity.

Andrews, (229) in a dermoid, found a tubular structure attached to a mesentery projecting into the cyst. It was gut, and even contained nerve ganglia in its coats.

Pye-Smith (230), in an infant, found two illformed but unmistakable feet in the cyst. They were covered with skin and showed heel, sole and toes (five on one and six on the other).

In contrast to the above instances, which illustrate fetuslike anlagen and especially the rare development of the lower trunk and extremities, the case of Saxer (231) is instructive. Here a well-formed premolar tooth lay loosely imbedded in a connective tissue capsule within an otherwise normal ovary.

STRUMA OVARII.—More regularly, thyroid tissue appears as the sole or main constituent of a teratomatous tumor. The absence of all other structures has been proved by serial section (Walthard, 232). Ascites is found in a large proportion of these cases, although the tumor is usually not malignant.

Gottschalk considered his case a "folliculoma malignum ovarii." Pick (233) pointed out the thyroid nature of the tumor and interpreted it as the one-sided development of this constituent or an overgrowth and destruction of the other elements by the thyroid tissue.

The writer (234) reported a case in which, with the expection of a well-developed tooth and a shell of bone, thyroid acini formed the entire growth

FIG. 290.—STRUMA OVARII. (×1.) Tumor cut across showing acini distended with colloid.

(Fig. 290). At that time only eleven cases were on record. The number had in 1918 passed 40 according to Adolph (235).

On section the tumor macroscopically and microscopically looks like colloid goiter. Brownish to honey-yellow cysts form a honeycomblike surface. Irregular cysts lined with a low cuboidal epithelium and filled with colloidal material are seen (Fig. 291). In one instance the iodine reaction proved positive.

In some cases the epithelium becomes multilayered and gives the appearance of a struma malignum. The writer has watched for over six years a patient from whom the late Dr. S. M. Brickner removed such a growth, and she has remained well.

Kretschmar's case (236) died of metastases. All others seem to have remained well.

Of the other structures recognizable by gross inspection the following require mention, hair, teeth, bones.

Hair.—The hair of a dermoid is usually collected in an almost inextricable tangled mass arising in a tuft from the plug. Blandin (quoted from Kroemer, l. c. 3, p. 214) found hair 3 meters long, blond at the tips, dark in the middle and white near their origin. All colorations are met with from the pigment-free, silvery white to darkest black. Lanugo hair is common. Pubic hair was found by Shattock (l. c. 228).

The tips of hair may penetrate any part of the cyst lining (like "ingrown" hairs). They then cause an inflammatory reaction which shows

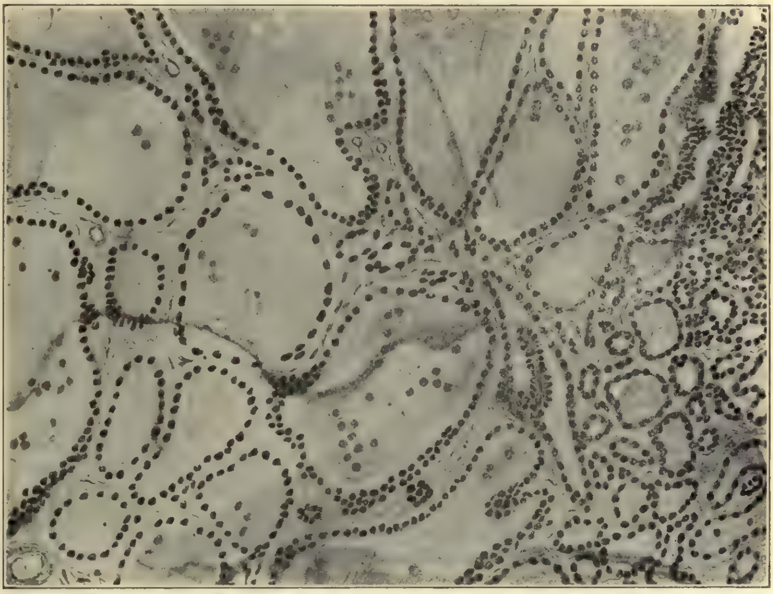

Fig. 291.—Struma ovarii. (Medium power.) The thyroid tissue (acini lined with low cuboidal epithelium) and the colloid contents are shown. Above and to the right the tissue resembles " fetal adenoma " of the thyroid.

itself by the formation of granulation tissue containing many foreign body giant cells.

Teeth.—These may be found projecting from the plug, or may be hidden in tooth sacs within the alveolus. They may be few in number, but as many as 300 have been found in one cyst. Usually they are attached to the rudimentary jaw-bone.

The teeth may be rudimentary and of fetal type, or well-developed with enamel, dentine, pulp and nerve fibers. They usually resemble canines and incisors and have one root, but the writer has seen molars. They may be pushed upward by developing teeth and drop loose into the cyst cavity.

Bones.—Usually the jaw bones are of undifferentiated form. Occasionally an upper jaw with antrum of Highmore, or a rudimentary lower jaw

with a coronoid process can be recognized. A petrous bone, an occipital bone with foramen magnum, ribs, pelvic bones, phalanges with three joints and a nail (Omori and Ikeda, 237), etc., are recorded.

Microscopic Appearance.—As most of the tissues to be mentioned closely conform to the normal structures of the adult, a brief description will suffice, emphasis being placed upon deviations from the normal.

Ectoderm.—The skin and its appendages closely resemble the adult type. The epidermis is thin but thickens in folds and nooks. Sebaceous glands are numerous, hypertrophic and in close apposition with hairs. The hairs arise deep in the subcutaneous fat, have a papilla and are pigmented (Fig. 292).

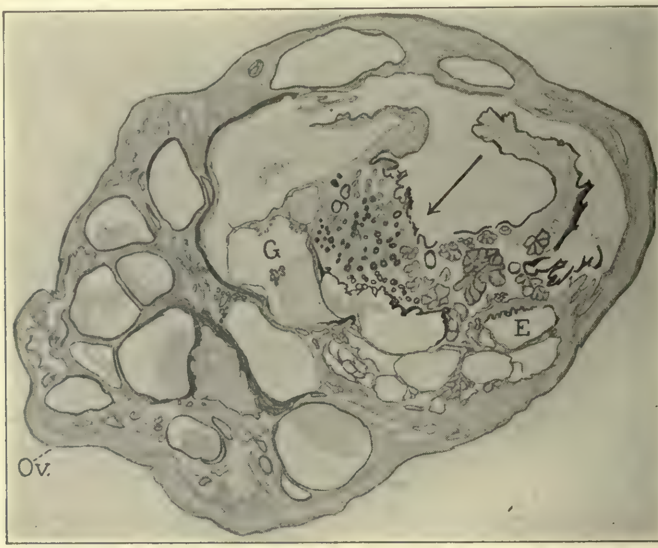

Fig. 292.—Embryoma of the ovary. (Very low power.) To the left is a cystic portion of the ovary (ov.). To the right is the embryoma. The arrow points to an area containing fair follicles (cut across), sebaceous and sweat glands. The epidermis is cornified (black). The cavity marked "E" is lined with high cylindrical epithelium (entoderm). The cavity marked "G" contains a pale area composed of glia and nerve cells. The convolutions within this cavity are a choroid plexus.

Arrectores pilorum muscles may be present. Sweat glands are few. The skin over the alveolus is of mucous membrane type. The teeth are usually normal.

Brain and Nerve Tissues.—These structures are more or less encapsulated in a fibrous sheath. Resemblances to cerebrum or cerebellum are rarely apparent (see Kroemer, l. c. 3, p. 226, Fig. 94). More often rosette-like neural tubes composed of neuro-epithelium (Wintersteiner's rosettes) and surrounded by glia are found. Pyramidal cells with axis-cylinders are very rare, while bipolar or unipolar ganglion cells and nerve fibers are commonly noted. A spinal cord with intervertebral ganglia was found in one

case. Convoluted choroid plexuses are frequent and prominent, projecting into ventriclelike cavities. Corpora amyloidea have been reported (Fig. 293).

The eye anlage may be rudimentary, single or bilateral, represented by choroidal pigment cells in some portion of a neural tube, or by a well-developed vesicle with clear fluid contents and pigmented lining. Cornea, eyelids and lashes have been reported, and in one instance a lens.

FIG. 293.—PLUG FROM A DERMOID CYST OF THE OVARY. (Low power.) 1. Hair follicles cut obliquely. 2. Sebaceous glands. 3. Epidermis. 4. Entoderm (ciliated, high columnar epithelium and goblet cells). 5. Cartilage. 6. Bone and marrow. 7. Nerve cells, glia; below this area are strands of nerve fibers.

Mammary gland with nipple, areola and gland structure is a great rarity (v. Velits, 238).

Entoderm is quantitatively not well represented. Such a find as a loop of intestine (Shattock, l. c. 228) is exceptional. Usually the structures are rudimentary. *The gastro-intestinal canal* appears in the form of cavities lined with a cylindrical ciliated epithelium. Usually the nuclei are basal. Goblet cells abound (Fig. 293). There may be well developed villi and solitary lymph-follicles. The cavity often shows unstriped muscle around its wall, also ganglion cells.

The respiratory tract, usually found in proximity to the preceding, is composed of a canal lined with stratified columnar ciliated epithelium. Acinous mucous glands and cartilage rings in its wall (Fig. 293) produce the semblance of a trachea.

Very frequently small undifferentiated cysts lined by an undifferentiated ciliated epithelium represent the entoderm.

Thyroid tissue close to the respiratory tract is not uncommon. Pick (l. c. 233) found it 6 times in 21 dermoids. The acini filled with colloid and lined by a single layer of low cuboid epithelium are characteristic.

Mesoderm.—The mesoderm is widely represented. In addition to the massive subcutaneous fat (Fig. 293), unstriped muscle is found in the walls of gut, of trachea, in the arrectores pilorum, etc. Striped muscle is uncommon (tongue), rudimentary heart muscle even more so (Katsurada, 239).

Cartilage, mainly hyaline, is a frequent find (Fig. 293) in the cranium, vertebrae, and in the trachea. Flat bones predominate, but long bones with fetal red and adult yellow marrow in their cavity occur (Fig. 293).

Well-developed blood vessels, which are in direct continuity with the vascular system of the host, abound. Lymph follicles occur in the gut segments and are scattered throughout the plug.

The lymph system is occasionally found injected when fat absorption is excessive (due to overproduction of sebum). Parts of the cyst wall, especially in the region of the ovarian rest, are converted into a porous, spongy mass with its interstices filled with an oily smear. The cystic spaces are lined by hyperplastic endothelium. Wolff (240) showed collections of dermoid fat in the broad ligament and in the mesenteriolum of the appendix resulting from such lymph transportation.

Endotheliomata are said to develop on the basis of such endothelial proliferations (?). Rössle (241) found a small lymphangioma in the ovary of a 10 months old child. Serial sections showed that it had arisen from the subcutaneous tissue of a minute dermoid.

Malignant changes in dermoids are not frequently reported in the literature. Frankl (242) recently stated that but 60 are on record. Yet Wiener (l. c. 90), in 60 dermoids, found 3 carcinomata, or 5 per cent. The condition must often be overlooked.

Carcinoma takes the form of squamous epithelioma of ripe form with pearl formation, arising directly from the epidermis of the plug. In a case operated upon by the writer the cancerous part formed a gelatinous appearing nodule in the cyst wall. The tumor had been noted 19 years and had started to grow rapidly for the last two years. Lung signs (metastases) developed several months after operation. Only in Yamagiva's case was the cancer of adenomatous type (mammary tissue). Spaulding's case (243) appears to be a basal cell epithelioma. Wolff (244) collected the literature to 1911, Eylenburg (245) reviewed 52 cases.

The *metastases* may be teratoid, carcinoma, or a simple tissue (as glia only) (Boxer, 246). Fat masses (usually also containing a few hairs)

may be encapsulated, forming *pseudo-metastases.* Distant metastases, as in the axillary glands, are uncommon (Clark, 247).

Carcinoma in the ovarian rest adjoining a dermoid has been described (Brettauer, 248).

Sarcoma is even less common than carcinoma. Only a few cases are on record and these are mainly melano-sarcomata arising from the pigmentary part of the anlage. Amann (249) described a black, grapelike tumor developing around a small dermoid; 1½ years later death from multiple metastases. Lorrain (250) reported a similar case, alveolar, round-cell, melanotic sarcoma.

Solid Teratoma (*Teratoblastoma*).—No hard or fast line can be drawn between the cystic dermoids and the solid (though polycystic) growths. In general it may be said that the tissues in the plug of a cystic teratoma have some semblance of purpose and arrangement and a tendency to form organs and organ complexes of the adult type. In solid teratomata, on the other hand, no definite arrangement, boundless proliferation and a more embryonal stage of development characterizes the tissues. Moreover, the embryonal mesoderm in particular shows excessive proliferative capacity. These tumors must be regarded as malignant.

FREQUENCY.—Teratomata are not frequent. In 1907 the writer (251) was able to collect only 37 well authenticated and 15 doubtful cases. Since then at least eleven more have appeared (Harris, Hörrmann, 252).

AGE.—The average age was 20 years, the youngest was 3¾ years, the oldest 40.

In Harris' case (252), in which the child was 5 years old, signs of precocious maturity developed and again disappeared after operation. He records ten cases in children under 14 years, which are not included in the writer's paper (l. c. 251).

Ascites is of frequent occurrence.

MACROSCOPIC APPEARANCE.—The tumors appear as massive solids, or polycystic growths with a thin, friable capsule. They may be nodular, or covered with innumerable grapelike appendages, or may have islands of skin with projecting hair on the surface. Adhesions are the rule and peritoneal implants are often found early.

Only in one case was the growth small and accidentally found at operation for a dermoid cyst of the opposite side (Frantzen, 253). Hörrmann's (l. c. 252) patient had a tumor weighing 10 kg. Most of the reports speak of tumors filling the abdomen.

On section innumerable small cysts, a marbled surface due to a conglomeration of tissues and hemorrhagic areas can be noted.

MICROSCOPIC APPEARANCE.—All the epithelial tissues noted in the dermoid plug may here be found scattered without order, undergoing uncountable reduplication and appear, as it were, fixed in a background of embryonal connective tissue (myxomalike, round cell or "sarcomalike").

In general the structures are more embryonal—the teeth still in the tooth sacs, the nerve tissues mainly glia and neural tubes, etc.; but more adult structures are also seen—nerve fibers, ganglion cells, hair, sebaceous glands, retina, choroid plexus.

The entoderm appears mainly as small cysts lined with undifferentiated, ciliated epithelium. The writer, however, found fairly well-developed intestinal tract in his case (l. c. 251).

The mesoderm shows fat, cartilage, bone, smooth muscle of embryonal type, but the main mass is composed of connective tissue. The septa are of the adult type but direct transitions to the embryonal can everywhere be traced.

This embryonal tissue is rich in cells and not unlike sarcoma tissue. The cells are small, round to spindle-shaped, with a distinct round nucleus and scanty cell bodies, which lie closely packed.

Many of the structures found in these solid teratomata defy classification. The cyst lining of the innumerable small cavities is indifferent epithelium.

No one tissue can usually be selected as the malignant element. The connective tissue, in spite of its sarcomalike appearance, is merely embryonal connective tissue. Neuroglia and neuro-epithelium is often preponderant.

Williams and Barris (l. c. 263, II, p. 768) have classified the case of Gosset and Masson as a *neuro-epithelioma* and recognize this form as a distinct variety.

More often, though still extremely rare, *chorionepithelium* overgrows the other tissues. Pick (254) described a case in which the tender age of the patient (9 years) precluded previous pregnancy and in which the presence of other ectodermal elements conclusively proved the teratomatous nature of the growth (Fig. 294). The chorionepithelium consisted of clear, glycogenic, polygonal, Langhans' cells, typical vacuolated and ciliated syncytium, which showed the intimate relationship to the blood channels and fibrin formation characteristic of these tumors. He calls these tumors chorionectodermal (Fig. 294).

Ries (255) describes a case and has collected six others from the literature. To these Kynoch's case (256) can be added. Unless absolute proof of virginity is obtainable the possibility of ectopic chorionepithelioma (see p. 473) or chorionepithelioma in a primary ovarian pregnancy cannot be excluded.

The cases all died except Ries' patient, who was alive seven months after operation.

Results and Cures.—Dermoid cysts are non-malignant tumors and 100 per cent of cures may be expected, except when carcinomatous changes occur and the cancer has passed the confines of the cyst.

Solid teratomas are most malignant. In the writer's series (l. c. 251)

of 37 cases the outcome was not known in 10. In the rest, a mortality of 88.8 per cent was assured and several cases had been observed only six months.

The average period of life after operation was ½ to 1¼ years.

Superficial dissemination over the entire peritoneal cavity was the rule. In only two cases was the pleural cavity invaded. In one the retroperitoneal glands were involved.

Metastases are composed mainly of mesoderm. In six cases, however, teratomatous metastases were found in the abdomen. In Ewald's case (257) the retroperitoneal glands also contained such complex deposits.

Histogenesis of Dermoid Cysts and Solid Teratomata.—Teratomatous growths were first observed in the ovary and hence Wilms (258) was led to consider these growths as limited to the gonads. He derived

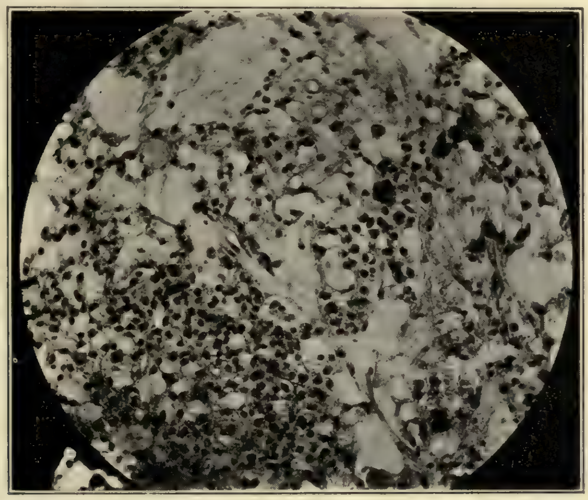

Fig. 294.—Chorionectodermal tumor of the ovary. (Photomicrograph.) (High power.) (Case of Prof. L. Pick of Berlin.)

their origin from the ovum by means of parthogenesis. However, teratomas containing all three layers have been found in such diverse locations as the pineal gland, the anterior mediastinum and the retroperitoneal tissues. Therefore any explanation to be convincing must apply to such tumors situated anywhere in the body.

The Marchand-Bonnet theory (221) accords genetic equality to parasites (fetus in fetu), dermoid cysts and teratomas wherever situated. A blastomere is cast out of the complex and retains the potentiality of forming a new individual if derived from the earliest cells, while this potentiality progressively decreases as the separation takes place at a later stage of embryonic development. The teratomatous tumor is a twin of its host.

What other factors enter in stimulating the quiescent blastomere to growth, and in one case produces a comparatively regular and organlike parasite, in another a dermoid

cyst with semblance of organoid, in still another a lawless and malignant teratoma, is not known. Furthermore, the development, instead of producing a three-layered growth (triphyllome), may be limited to two layers, ectoderm and mesoderm (biphyllome). Overgrowth of one tissue may produce apparently simple tumors (struma ovarii, epithelioma chorionectodermale, etc.).

The literature of this interesting subject will be found in Pfannenstiel, Veit's Handbuch, IV, i, p. 282.

HYPERNEPHROMA OF THE OVARY

Adrenal rests (Marchand's) may be found in the ovary. From these, typical Grawitz tumors may originate. However, it must not be forgotten that a latent kidney tumor may produce metastases in the ovary, or tumors from the broad ligament may invade the ovary (Alamartine and Maurizot, 259).

These authors mention that of 10 genital cases 3 were in the broad ligament, 5 ovarian and 2 bilaterally ovarian. All the followed-up cases died with development of metastases.

The growths are large, solid tumors with hemorrhages, necrosis and cyst formation. The color is yellow or yellowish pink. In an edematous stroma, usually in close relation to capillaries, are long rows of large, clear, cubic or polygonal cells with a vesicular nucleus and dark nucleolus. The cells contain fat (lipoid) and glycogen. For literature see Pick (260).

FOREIGN BODIES IN THE OVARY

Two cases of needles embedded in inflamed ovaries are recorded by Gebhard (l. c. 38, p. 396). The one was supposedly due to being swallowed, the other was perhaps inserted per vaginam in an attempt to induce abortion.

PARASITES

Ecchinococcus.—Primary ecchinococcus of the ovary is most infrequent.

Bland-Sutton (261) regards all ovarian cases as secondary. However, Péan (262), and Taylor and Welsh (263) removed tumors which were in the ovarian stroma and perhaps primary. Freund (264) found an echinococcus of the omentum which had broken through into an ovarian cyst. More often the primary seat is in the broad ligament or pelvic connective tissue. For literature see Pfannenstiel, Veit's Handbuch IV, i, p. 105.

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CHAPTER XI

PAROVARIUM

The parovarium or epoöphoron is a comblike structure which lies between the layers of the broad ligament in the portion situated between tube and ovary. The back of the comb is formed by the thicker part, which corresponds to the wolffian duct, the teeth—some 4 to 10 in number—to the smaller ducts which run toward the hilus of the ovary (Fig. 15, p. 27). The small ducts do not connect with the main channel, but end blindly a few millimeters from it by bending at a sharp angle and then running for a short distance toward the uterus.

The degree of development of the parovarium is very variable. The ducts consist of a tube surrounded by a thick layer of unstriped muscle and lined by cuboidal or low cylindrical ciliated epithelium (Figs. 57–8).

The parovarium attracts attention only when it is the seat of a growth. These growths are almost invariably simple (retention) cysts, although true proliferating cystic neoplasms are also on record.

Frequency.—Wiener (l. c. 90, Chapter X) found 4.1 per cent, Wichmann (1) 8.6 per cent, Hoehne (l. c. 156, Chapter X) 10.1 per cent of parovarian cysts among ovarian neoplasms.

Age.—They occur most frequently, according to Wichmann (l. c. 1), who examined 53 cases, between the twentieth and thirtieth years.

Macroscopic Appearance.—Cysts, usually single and unilocular, which may be of minute size or attain enormous proportions, arise between tube and ovary. Many of the cysts become pedunculated, the tube, broad ligament and ovarian ligaments forming the broad pedicle. Very rarely they develop only in a downward direction, becoming truly retroperitoneal. The tube encircles the cyst and together with the ovarian fimbrium may be much elongated (Payer, l. c. 15, Chapter IX, 76 cm.).

The cysts are usually very thin-walled and flaccid. Güttler (2) removed one weighing 53 kg. and Nagel (3) one containing 33 liters of fluid.

It may be difficult in large cysts to prove the origin from the parovarium. The presence of the intact ovary, the peculiar relation of the tube, and two layers of independent vessels (one on the wall of the cyst, the other in the loose, covering peritoneum) are corroborative.

The cyst fluid, unless contaminated by blood, is clear, watery, faintly alkaline, of low S. G. (1.005 to 1.010) and contains only a trace of albumin, but no mucin or pseudomucin.

The wall of the cyst is thin, fibrous, lined by a glistening layer, usually

smooth, but in some cases thrown into folds or with localized areas of low papillae. These papillations are either warty, or if edematous, hydatid in form (about 30 per cent are papillary, Wichmann (1), Wiener (l. c. 90, Chapter X).

Torsion of the pedicle has been noted not infrequently. Lenzi (4) collected 41 cases from the literature and added 3 of his own. Rosenstein (5) reported a case where the ovary was slowly cut in two by persistent torsion, v. Derera (6) where the sigmoid was incarcerated and became gangrenous.

Microscopic Appearance.—The cyst wall is formed of fairly cellular connective tissue. Occasional unstriped muscle fibers are found in the wall, and there is, according to Wichmann (l. c. 1) an unusually large amount of elastic tissue.

The lining epithelium consists of a single layer of cuboidal or low cylindrical cells, which, in the fresh state, show well-marked cilia. Rarely the cells are flat and endothelial in type.

The papillae are low and covered by the unchanged epithelial lining, as in the follicle cysts.

A few other solid and cystic neoplasms have been described. Pick (7) reported a bilateral fibroadenoma of the parovarium, of the type of v. Recklingshausen tubal growths (see Chapter IX, p. 345).

Falk (8) describes a recurrent papillary growth.

Goldschmitt (9) and Spanton (10) reported sarcoma in the wall of parovarian cysts.

Dermoids have been reported by Zaccharias (11) and Häfner (12).

Cancer has also occurred in parovarian cysts, both primary and metastatic (Schottländer, Talmey, 13).

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CHAPTER XII

PELVIC CONNECTIVE TISSUE

The distribution of the fibrous, fatty and unstriped muscle tissue, which surrounds the subperitoneal portions of pelvic viscera, has been described under the anatomy of prolapse (see Chapter VII, p. 166, and Fig. 116). The diseases of these tissues, in the main, are dealt with together with the lesions of the various genital organs which they surround. A few additional facts require discussion.

Anatomy.—The extent and distribution of the pelvic connective tissue spaces has been studied by means of the injection of soft or fluid masses. Without entering into minuter details it may be stated that three zones are readily demonstrable—a para-vesical, para-cervical and para-rectal one. Extension downward proceeds along the vesicovaginal, rectovaginal or para-rectal tissues; extension upward in the anterior space of Retzius, extraperitoneally above Poupart's ligament, and along the flare of the ilium, and retroperitoneally along the psoas muscle to the kidney region. For details see R. Freund (Veit's Handbuch der Gynäkologie, 1912, Vol. V, p. 336).

Hematoma of the pelvic cellular tissues may occur above the muscular diaphragm, below it or communicating by means of various weak spots and gaps, above and below combined. The main sources of hematomata have been discussed under Vulva (p. 103), Vagina (p. 137), Uterus (p. 179), Ectopic Pregnancy (intraligamentary) (p. 454).

Williams (1) has collected 33 cases of subperitoneal hematoma occurring post partum without rupture of the uterus. Often the labor is spontaneous. The mortality was 56 per cent. Beck (2) was able to find 177 cases in the literature, of which only 11 were puerperal.

Patients may bleed to death into their own cellular tissues, the hematoma may rupture into the vagina or peritoneal cavity. Infection and abscess formation may result. Most often absorption and recovery takes place. Hematomas are common after pubiotomy and gynecological operations. Hematoma of the round ligament occurs.

Varicocele of the broad ligament has been described. It is most often a sequel to fibroids of the uterus but may be idiopathic (Shober, 3). Phleboliths in the pelvic veins may be confused with ureteral stones (Clark, 4).

Infection of the cellular tissues is always of bacterial origin. The result is a phlegmon which may be localized or diffuse. Depending upon the nature of the invading germ, the resistance of the patient, the point of origin and complicating factors (birth injuries, pyosalpinx, etc.) protean manifestations result, which, however, by analysis, can be reduced to simple factors.

Etiology.—Every trauma of the vulva, vagina and cervix complicated by breaks in the epithelial surface, affords points of entry for germs into the paracolpium and parametrium. The gonococcus may penetrate through the intact mucosa, and the colon bacillus can pass through the rectal wall. Bacteria penetrate the walls of the inflamed veins and lymphatics in puerperal infections (p. 482) and set up a diffuse inflammation of the cellular tissues surrounding the vessel walls. Finally, diseased adnexa may, after forming adhesions to the broad ligament and pelvic peritoneum, by continuity, infect the cellular tissues, or the infection may proceed through the mesosalpinx or mesovarium.

From one-half to three-quarters of all cellular infections are due to puerperal causes (post-abortive and post-partum). A large number of the remainder result from intra-uterine manipulation (curettage, intra-uterine applications), cervical dilatation and the use of cervical anticonceptional devices. A smaller number are due to extension from adnexal disease, breaking down of uterine new growths and operative infections.

Gross Anatomy.—*In acute infections* a rapidly spreading exudation takes place, producing paravesical, parametritic and pararectal (or combinations) masses which distend the subperitoneal tissues, either pushing the viscera toward one side if unilateral, or depressing or elevating them if bilateral. On incising the exudate a pale, watery tissue is encountered from which a colorless fluid exudes. The fluid, as well as the tissues, contain bacteria, pus, round and plasma cells.

At a later stage the exudate is harder, the viscera being enclosed in a plasterlike cast, which may extend on the iliac flare, above Poupart's ligament, etc. (see Prolapse, p. 166). Incision demonstrates cloudy and flaky fluid and pus in the lymph vessels, thrombi in the smaller veins, and widely scattered minute abscesses in the meshes of the connective tissue.

Resolution may take place with almost complete restitutio ad integrum. Gangrene of tissue may develop. The abscesses may coalesce, forming larger abscesses. These abscesses may inspissate and calcify. More commonly they burrow, and if undrained, eventually empty into adjacent hollow organs (bladder, rectum, vagina) or perforate the skin above Poupart's ligament, or in the saphenous (through the femoral canal), or gluteal (through sciatic notch) region. Very rarely abscesses burst into the peritoneal cavity. After healing, dense parametrial scars, with consequent displacement (by traction) of the generative organs, remain. In fatal cases wide spread changes are found throughout the viscera (cloudy swelling of kidneys, splenic tumor, etc.).

The writer saw a case of lymphangitis of the round ligament, arising in the course of an acute gonorrhea. An exudate in the inguinal canal developed and was slowly absorbed.

Similarly, localized exudates may form in the broad ligament, of which "stump" exudates after operation are the most frequent example.

Chronic infections, especially of localized areas, such as of the sacro-uterine ligaments, are of frequent occurrence. Infiltration, followed by atrophy of the elastic and muscle elements, produces scars and retraction. *Parametritis chronica atrophicans* of W. A. Freund is a symptom complex in which the entire genital system, including uterus, vagina, adnexa and connective tissues undergo premature senile atrophy. The resulting disturbances are at first most evident in the parametria. Cachexia, endocrine disturbances or too frequent childbirth, may be causative.

Tuberculosis, syphilis, actinomycosis may produce specific infections of the cellular tissues in connection with infection of other genital organs. See these diseases under Vulva, Vagina, Uterus, Tubes and Ovaries.

New Growths.—Ovarian cysts become secondarily intraligamentous by development and extension (see p. 384), but parovarian cysts are primarily subserous. This applies as well to cysts of Gärtner's duct (see Vulva, p. 115, Vagina, p. 146, and Cervix, p. 66).

A large lymph cyst (Lion, 5) of the broad ligament in a child of 3½ years remains unique.

Epidermoid and dermoid cysts are described under teratomatous growths.

Hydrocele of the canal of Nuck may simulate a true cyst (see Vulva, p. 114). A few cysts of the round ligament are recorded (Emanuel, 6).

Fibromyoma; Adenomyoma.—Intraligamentous tumors may, by upward growth, produce a *pedunculated* type, or if retroperitoneal, grow between the layers of the cecum and sigmoid colon—sessile. Downward enlargement may extend retroperitoneally toward the vulva, perineum, and gluteal region (through the sciatic notch) or into the hollow of the sacrum.

Pedunculated growths may undergo torsion (Cullingworth, 7), and produce ascites.

Lateral or upward displacement of the bladder and uterus, slitlike compression of the rectum, and displacement of the ureter are important sequels.

Fibromyomata are infrequent. Strohecker (8), who did not exclude cases becoming secondarily intraligamentous, was able to gather only 204 cases in 1902. Steele (9) reported a tumor weighing 20 pounds. The growths are usually unilateral. In addition to tumors situated merely subperitoneally, an origin from a definite part of the cellular tissues can be demonstrated in some cases. Thus tumors of the round, ovarian and sacrouterine ligaments have been described.

Fibromyomata of the round ligament occur in the intraperitoneal course of the ligament, intra-canalicularly or extra-abdominally (pre-

inguinal). Of 76 round ligament tumors Emanuel (6) found 61 extraperitoneally and only 19 intra-abdominally developed. Hirst and Knipe (10) were able to collect 41 fibromyomata.

The round ligament usually spreads out over the tumor, which is composed of unstriped muscle and connective tissue. These growths may undergo the same degenerations as uterine fibroids (see p. 247), including sarcomatous changes.

Adenomyoma may also occur (see Adenomyoma, p. 213).

Martin (quoted by Emanuel) removed a tumor containing 12 liters of chocolate-colored fluid, probably due to cystic distention of an adenomyoma of the round ligament.

Fibromyomata of the infundibulopelvic and *utero-ovarian ligaments* are recorded (see Emanuel, l. c. 6).

Lipoma is a rare growth unless lipomata growing secondarily downward into the pelvis from between the layers of the mesentery are included.

Freund (l. c. 8, p. 534) excludes all but two cases (Pernice-Middelschulte and Borrmann-Friese). In the first case the tumor weighed 15 kg. Rarely, small fat tumors of the round ligament (pre-inguinal) are found.

Tumors secondarily intraligamentous, may grow down from the mesentery, or arise from extra-peritoneal fat, and enter the pelvis through the sciatic or obturator foramen. Recurrences have occurred (Johnstone, 11).

For liposarcoma see the next paragraph.

Sarcoma of the pelvic connective tissue is rare. Freund (l. c. 8, p. 532) was able to collect 32, which includes 4 of the round ligament. These tumors resemble fibromyomata early in their course but later show invasive tendencies and may metastasize (Takeyoshi (12), thyroid metastasis).

Degenerations, pseudocyst formation, and hemorrhages occur. The tumors described are intraligamentous, paravaginal, round ligament, etc.

All histological varieties from the well differentiated "myoma malignum" to small, round-cell sarcoma are described.

Of 34 cases, 9 were fibrosarcoma, 8 spindle-cell sarcoma, 5 myoma malignum (all round ligament growths), 5 round-cell, 3 telangiectatic sarcoma, 2 contained giant cells, 1 chondrosarcoma, 1 liposarcoma.

Of 37 cases 25 were in the broad ligament, 6 arose from the round ligament, 3 paravaginal, 2 precervical, 1 in the vesicovaginal septum.

Of 40 cases the outcome was not mentioned in 7. Of the remaining 33 cases 13 were discharged cured, further fate not stated, 10 died in consequence of the operation and 10 showed recurrences or died within ¾ of a year.

Teratoma; Dermoid Cysts.—Dermoid cysts are uncommon. R. Freund (l. c. 8, p. 538) mentions only 33. Both ovaries must be found intact and bearing no relation to the cyst. The presence of an accessory or supernumerary ovary can never be definitely disproved.

The most frequent site is in the paraprocteum between rectum and sacrum, next the base of the broad ligament, the retrocervical tissues below Douglas' cul-de-sac, and the round ligament. The tumors rarely grow larger than a child's head. Their make up is usually simple. In only five did hair occur, bone in four. Instead of the atheromatous dermoid contents, a "café au lait" or chocolate-brown fluid may be evacuated. Teeth have been reported.

The tumors have caused dystocia. Some have become infected.

For literature see Reinecke, Germain (13).

Tumors from Embryonal Rests.—(*a*) From the epoöphoron—parovarian cysts, etc., see Chapter XI, p. 437. (*b*) From the wolffian duct (Gärtner's duct) which include cysts (see Vulva, Vagina, Cervix), adenoma and carcinoma (R. Meyer, 14), two cases. (*c*) From pronephric rests (?), small, epithelial, pearlike formations in the anterior layer of the broad ligament. They may acquire a cystic lumen but do not form dermoids.

Echinococcus.—According to Young and Welsh (15) the great majority of primary hydatids of the pelvis take origin in the connective tissue immediately beneath the peritoneum of Douglas' pouch. Secondary implantations in the cul-de-sac occur when hydatid cysts (especially hepatic ones) rupture into the peritoneal cavity, the cyst content gravitating to the bottom of the pouch. When numerous and massive cysts surround and invade the various pelvic organs and riddle the connective tissue, the point of origin can no longer be determined.

The cysts may spread into the precervical region (Haupt, 16), upward along the anterior abdominal wall, downward to the perineum or ischiorectal fossa, or into the thigh through the femoral or sciatic canals. Pararectal development is frequent. Growth is slow except during pregnancy. Suppuration may develop. Rupture into neighboring hollow viscera has occurred—rectum, uterus, bladder, vagina—with expulsion of parts of the membrane, entire vesicles, or clear, non-albuminous fluid containing scolices.

The echinococcus capsule consists of lamellated connective tissue, which may contain calcified areas. The surrounding tissues are inflamed and hyperemic.

For literature see Freund (l. c. 8, p. 567).

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CHAPTER XIII

OBSTETRIC PATHOLOGY

To deal adequately with this large subject would require a separate volume. Here only a short résumé will be given, with the exception of two subjects which will receive more detailed treatment, namely, extra-uterine pregnancy and chorion epithelioma.

Normal pregnancy has been discussed in Chapter IV. The reader is referred to this exposition in order that he may fully understand deviations from the normal.

EXTRA-UTERINE PREGNANCY

The pregnancy may be normal except in the site of nidation. Extra-uterine pregnancy includes tubal, fimbrial, ovarian, tubo-ovarian, peritoneal and secondary abdominal. Abnormally low nidation produces placenta previa and cervical pregnancy, which are, however, intra-uterine.

Causes.—Any cause which arrests or retards the downward progress of the fertilized ovum sufficiently to allow the egg to acquire its lytic power before it reaches the uterus favors an ectopic gestation.

Foremost among the causes is inflammation—loss of cilia in the mucosa, agglutination of folds, diverticula due to salpingitis nodosa, kinks the result of perisalpingitis, very rarely acute salpingitis (Hitschmann, 1).

Congenital diverticula (Huffman, 2), tumors in the tubal lumen (Outerbridge, 3), external migration of the ovum, are less frequent causes.

Whether Webster's hypothesis that the ovum can embed only in tissue derived from müllerian derivatives has any foundation in fact remains unanswered (see Adenomyoma, Chapter VII, p. 214).

Frequency.—Extra-uterine pregnancy is of frequent occurrence. Its absolute frequency as compared to intra-uterine pregnancy was recently determined by Schumann (4) giving a ratio of 1 to 202. Farrar (5), in 309 cases, found ectopic representing 1.5 per cent of gynecological patients, Wynne's (6) 303 cases representing 1.3 per cent.

Age.—The writer (7), in 80 cases, found the age distribution as follows:

15 to 20	1	35 to 40	13
20 to 25	20	40	2
25 to 30	20	Unknown	3
30 to 35	21		

This signifies that 76 per cent occur between the ages of 20 and 35 years. Farrar (l. c. 5) found 63 per cent between 24 and 33 years.

Site.—According to the primary site of embedding we distinguish in tubal pregnancy, interstitial, isthmic and ampullar. Secondarily by growth, rupture, etc., further subvarieties such as tubo-uterine, intraligamentous, tubo-abdominal and secondary abdominal may develop.

Foskett (8), in 117 cases, found:

Ampullar	52
Isthmic	64
Interstitial	1

The writer (l. c. 7), among 80 cases, to which later 25 new ones were added (unpublished), found 1 intraligamentous, 2 abdominal (secondarily).

Tubo-ovarian, ovarian and peritoneal pregnancies are too infrequent to be numerically classified.

Nidation.—In the Tube.—The ovum behaves exactly as in the uterus, such differences as develop arise from the difference in the structure of the tube.

The ovum may burrow into a tubal fold (columnar) or between folds (intercolumnar) or in a false passage, diverticulum or accessory tube (Eckler, 9). The thin mucosa offers little resistance to the erosive action of the trophoblast. Therefore erosion of the muscle occurs early and the ovum lies either in the musculature or between muscle and mucous membrane.

The tubal lumen usually is distorted, compressed and becomes slitlike. The trophoblast may then erode both layers of mucosa, which are now in apposition and the ovum appears centrally implanted (Figs. 295–6). More often in the early stage the mucosa forms part of an imperfect decidua capsularis.

Decidua formation is imperfect in the tube. Instead of the thick, continuous uterine decidua with its distinct layers, only a weak reaction, often limited to a few tubal folds and to the walls or vicinity of the blood vessels can be found. According to Kermauner (10) decidua forms in about 15 per cent of cases in the tube (Figs. 297 and 298).

The absence of decidua affords the trophoblast unresisted advance, which evidences itself by erosion of the muscle and invasion of the maternal veins for long distances (Hitschmann, 11). The erosion is, however, to a certain degree, self-limited because the fibrin derived from the blood, which accumulates around the shell of trophoblast, and the partly digested

maternal tissues form a resisting zone. If the pregnancy is not terminated by one of the many accidents to which it is subject (see p. 452) before a placenta is formed, further progress is not interfered with by trophoblastic

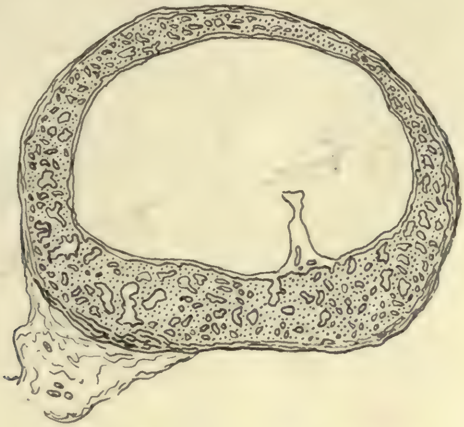

FIG. 295.—TRANSVERSE SECTION THROUGH A FALLOPIAN TUBE CONTAINING A SIX-WEEKS' UNRUPTURED ECTOPIC PREGNANCY. (×4.) Centrally is the amniotic cavity into which projects the stump of the umbilical cord (embryo of 9 mm. removed). The chorion is still diffuse, though the future placental site is well developed toward the mesosalpinx. No evidence of tubal lumen remains. The tubal wall is much thinned.

FIG. 296.—ENLARGED PART OF PRECEDING FIGURE 295. (×20.) 1. Umbilical cord. 2. Blood in intervillous space. 3. Villus. 4. Fibrin streak, note absence of decidua. 5. Thinned tubal wall.

erosion, for the formed placenta no longer has an erosive action. After the placental stage is reached, accidents are due to inability of the tube to dilate enough to accommodate the products of conception.

Uterine decidua appears to form in the majority of cases (Fig. 299),

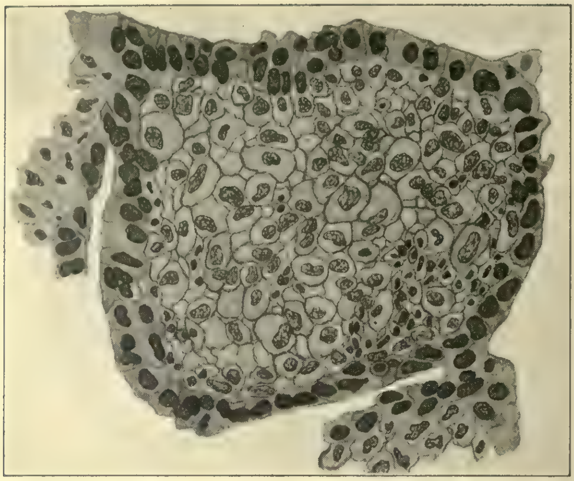

FIG. 297.—TUBAL FOLD ONE INCH FROM AN ECTOPIC SAC. (High power.) Marked decidua reaction of the stroma of the fold. The surface epithelium is high and succulent.

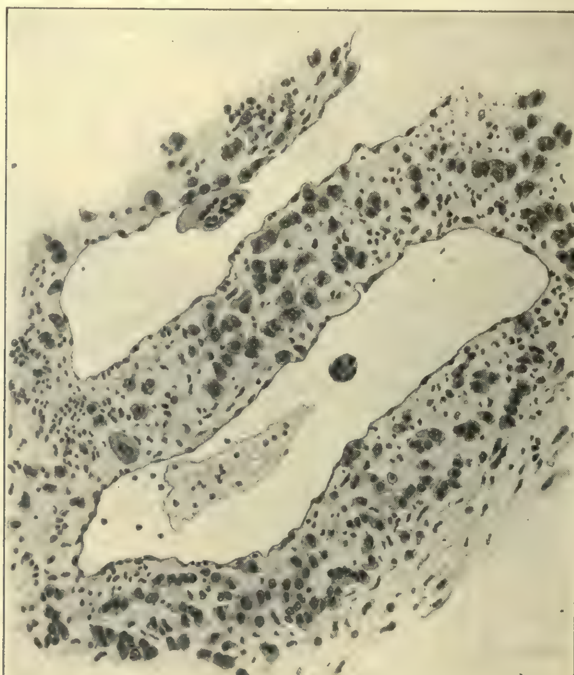

FIG. 298.—AN ARTERY AND A VEIN OF A TUBE, FAR FROM THE PLACENTAL SITE OF A TUBAL PREGNANCY. (High power.) Note the marked decidual changes in the vessel walls. Syncytium is seen in both the lumina.

but is passed in the form of a triangular cast (see p. 191) in only a small number of instances. After termination of the tubal pregnancy the uterine

FIG. 299.—UTERINE DECIDUA IN TUBAL PREGNANCY. (Photomicrograph.) (Medium power.)

decidua can regress in situ. The uterine changes produce the bleeding from the vagina noted in ectopic pregnancy (Sampson, 12).

Abdominal decidua is more common in ectopic than in uterine pregnancy. Care must be taken not to confuse inflammatory (especially pseudoxanthoma cells, see p. 339) with decidual reaction. The commoner sites

are omentum, appendix (Figs. 300 and 301), surface of the ovary, pelvic peritoneum. For literature see Taussig (13).

FIG. 300.—TRANSVERSE SECTION OF THE APPENDIX VERMIFORMIS. (From a case of Tubal Pregnancy.) (×9.)

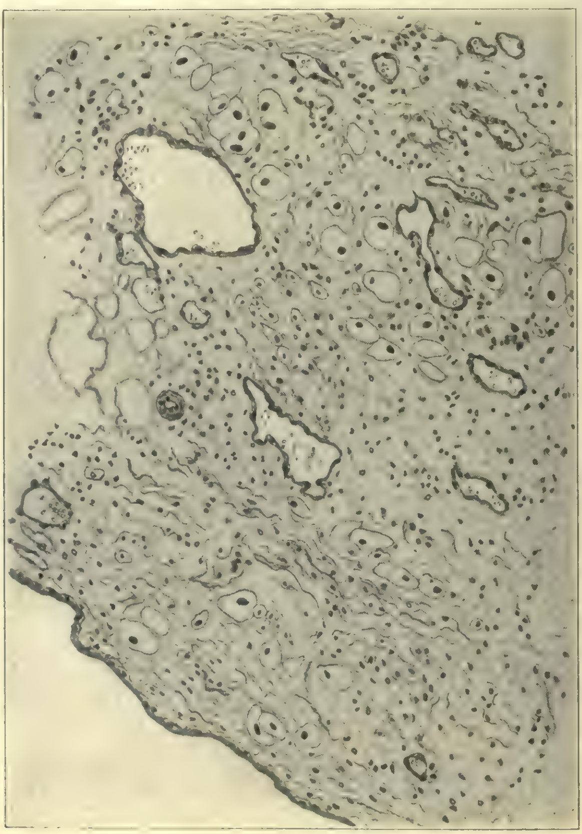

FIG. 301.—HIGH POWER OF BOXED-IN AREA OF FIG. 300. DECIDUAL REACTION IN THE APPENDIX. This area, from the outer layer, shows marked decidual changes in the stroma. Note the large, clear decidual cells. (Case of Dr. E. Moschcowitz.)

In the Ovary.—Norris (14) was able to collect 19 cases of primary ovarian pregnancy by 1911. Rubin's case (15) was the twenty-first. Since then a considerable number of new ones have been added. The site of nidation appears to be in the graafian follicle although implantation in the stroma is also described.

Early cases alone can be used in deciding upon the mode of nidation. As the pregnancy advances the erosive trophoblast burrows beyond the follicle and the nidation then appears to be stromal. Decidua formation is even more imperfect than in the tube. The ovary shows a surprising capacity for enlargement and distention.

In advanced cases, to determine an ovarian pregnancy, not only must the sac occupy the site of the ovary (connection with the uterus by the utero-ovarian ligament), but ovarian tissue must be found in various points of the sac and the tube, on the affected side, must show no macroscopic or microscopic evidence of pregnancy (Norris, l. c. 14).

On the Peritoneum.—Primary peritoneal pregnancy is scouted by some. If not primary, a most early secondary abdominal pregnancy is described by Hirst and Knipe (16) situated on the posterior surface of the broad ligament. Hammacher's case (17) was on the serosa of the tube.

In more advanced pregnancies the origin can no longer be determined with accuracy as, for example, a primary tubal site, might in time clear up, so as to show no evidence even to the microscope.

Fimbrial, tubo-abdominal and *tubo-ovarian* (in a tubo-ovarian cyst, Zahn, v. Ehrlach, see Kroemer, 18), implantations may occur, but probably in most instances are primarily tubal.

Macroscopic Appearance.—An *unruptured* tubal pregnancy may present an elastic, beadlike enlargement anywhere in the course of the tube.

The tube is usually deep red, congested and succulent. In the rare instances in which the tube dilates without rupture, to accommodate an advanced pregnancy, the musculature is greatly thinned out.

Tubal rupture may be limited to a minute hole through which a blood clot or the fine villi project, or large tears or punched-out defects may exist. At operation a spurting artery may be found. Tears in the walls of the sac in advanced pregnancies may occur, through which fetus or placenta or both may extrude.

In tubal abortion the enlarged tube dips into a more or less encapsulated hematocele. As organization proceeds the blood clots are firmly walled off by a connective tissue membrane, beyond which are the closely adherent intestinal loops and other adjacent viscera.

Ovarian pregnancy appears as a hematoma of the ovary. Later a large mass is found in the ovarian region and microscopic examination of the walls of the sac alone can assure the diagnosis of ovarian origin.

In *abdominal pregnancy*, whether secondary or primary, the fetus is found in its amniotic sac, the intestine, mesentery and abdominal viscera forming the wall (Fig. 302). The placenta may remain in the tube, communication being maintained solely by the cord, or the placenta may be attached to almost any of the abdominal viscera (Fig. 303).

Microscopic Appearance.—This has been discussed under Nidation (p. 446). In every instance villi must be found to confirm the diagnosis unless a fetus is present. The decidual reaction will be most evident in portions of the tube at a slight distance away from the fetal sac. (See Fig. 297.)

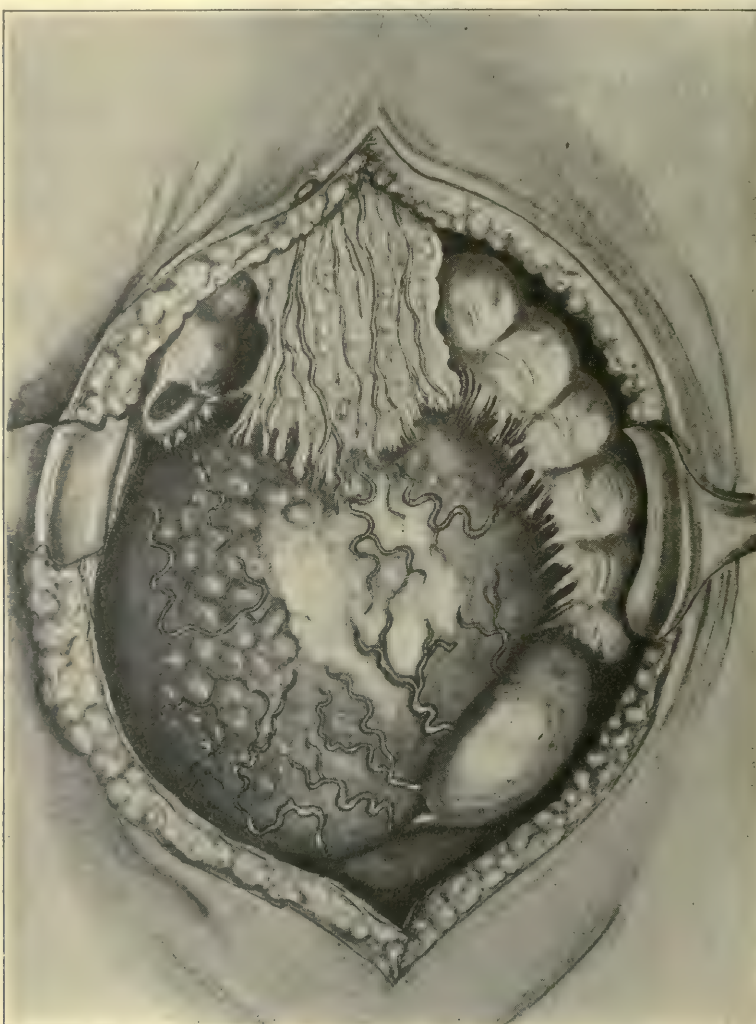

FIG. 302.—UNRUPTURED ABDOMINAL PREGNANCY (SECONDARY). Fetus 27 cm. long. The sac lies behind and to the right of the uterus. From right to left of the patient, cecum, appendix, omentum and sigmoid help to shut off the sac.

The outcome of an ectopic pregnancy depends upon various factors. The site of implantation has much to do with it. In tubal pregnancy the commonest outcome is tubal rupture with hemorrhage, or tubal abortion, either with diffuse peritoneal hemorrhage or with a localized peritubal hematocele formation.

In 105 cases the writer (l. c. 7) found 53 ruptures, 31 abortions, 12 hematoceles, 5 unruptured tubal pregnancies, 1 intraligamentary rupture, 2 abdominal pregnancies, 1 combined extra- and intra-uterine pregnancy. Farrar's (l. c. 5) series showed an even higher percentage of ruptures to abortions, 169 to 81.

Before tubal pregnancy was recognized and operated upon, 69 to 95 per cent of the women with ectopic pregnancy died from hemorrhage

FIG. 303.—SHOWS ATTACHMENT OF THE PLACENTA FROM FIG. 302. The placenta is attached to the posterior surface of the broad ligament and the lateral pelvic wall. Remains of a peritubal clot adheres to the abdominal end of the right tube.

(Schauta, 19). In a small number hematocele, lithopedion formation, retention, or expulsion via an abdominal sinus or through rectum or bladder brought about a cure. To-day more than 95 per cent recover (Frank (l. c. 7), 3.8 per cent; Farrar (l. c. 5), 0.97 per cent of deaths).

An interstitial pregnancy may rarely grow inward and become uterine. Probably many of the so-called "cornual" pregnancies are interstitial at the outset. Usually the unyielding musculature of the interstitial part of the tube ruptures early. Interstitial pregnancy is easily overlooked at operation

unless searched for. The writer recalls a case where the source of profuse intra-abdominal hemorrhage was not found at operation because the uterine portion of the tube had not been examined. At autopsy a minute rent was noted within the uterine wall.

Isthmic nidation most commonly ends in tubal rupture. Tubal abortion does, however, occur in this variety. In rupture the opening in the tubal wall may be minute. Sometimes large defects result from erosion, necrosis and the explosive force of the bleeding.

Ampullar pregnancy most commonly ends as a tubal abortion. Gradual rupture into the wide tubal lumen is followed by bleeding into the tube. The blood partly clots and is extruded into the abdomen. Repeated hemorrhages produce a *peritubal hematoma or hematocele.*

The blood clots and fluid blood are encapsulated by peritoneal adhesions. The site is most often behind the uterus in Douglas' cul-de-sac, but small collections may form anywhere in the true and false pelvis, at the root of the mesentery, in the iliac fossa or between coils of intestine, wherever the end of the tube may be situated. The fimbriated extremity of the tube commonly ends in the hematocele wall and the fimbriae may be spread out on the inner surface of the wall, forming a rosette when viewed from within.

The wall of an hematocele is first composed of lamellated fibrin and is later replaced by connective tissue. All adjacent viscera are intimately adherent to the wall.

The extrusion of the ovum from the tube does not necessarily signify the death of the ovum. Secondary implantation in the hematocele and the danger of secondary rupture of this mass, though uncommon, must not be forgotten (Fig. 304).

An hematocele may absorb; if small this outcome is possible. The process is slow and usually incomplete, adhesions about the tube remaining.

Suppuration, with the formation of a pelvic abscess and perforation into vagina, bladder, rectum and with ultimate cure, was frequent in the preoperative era. Perforation into the free peritoneal cavity also occurs.

The fate of the fetus varies. If rupture or tubal abortion with termination of the pregnancy occurs in the early weeks and the patient survives, the fetus is absorbed. In the later months the fetus in pregnancies which terminate unoperated, dies and is retained for many years (up to 50 years) becoming encrusted with lime salts—lithopedion (Bainbridge, 20) (Fig. 305), being partly absorbed, and only represented by fatty matter (adipocere) or being skeletonized, the fetal bones being retained or eventually expelled through fistulae leading to the surface (abdominal wall, bladder, rectum, etc.).

In a certain small number of cases, live, viable fetuses are obtained by operation (S. Horsley, Beck, 21). Beck was able to collect only 262 cases with live fetuses (after the fifth month). If ectopic pregnancy is first

seen or recognized late, it is justifiable to wait, for instance from the 36th to the 38th week in the interest of the child.

OTHER TERMINATIONS.—A *tubal mole,* similar to a uterine mole (see p. 462) may form at the implantation site consequent to small repeated hemorrhages. Moles can be completely absorbed or may calcify (Maxwell, 22).

A hydatid molar pregnancy may occur in an ectopic location. A number of such instances are recorded (see p. 470).

Chorionepithelioma as a sequel to tubal pregnancy is reported. The case of chorionepithelioma in the region of the sacro-uterine ligament, reported by the writer (23), may have originated from a peritoneal pregnancy.

FIG. 304.—EARLY STAGE OF SECONDARY ABDOMINAL PREGNANCY WITH SUBSEQUENT RUPTURE AND HEMORRHAGE. 1. Uterus. 2. Left normal tube. 3. Back of fetus seen through the membranes. 4. Upper edge of the placenta. 5. Secondary hemorrhage (clots). 6. Enlarged tube, in which the pregnancy originated.

Coincidence of extra- and intra-uterine pregnancy cannot be very unusual. In a series of 105 cases the writer found it once. Simpson (24) collected 113 cases up to 1904 (of these 98 were coincident; in 16 the ectopic gestation was dead when the intra-uterine conception took place; in 3 the ectopic preceded the intra-uterine implantation).

Bilateral tubal pregnancy is a great rarity. Unterberger (25) collected 16 cases, while Proust and Buguet (26) accept as genuine only 33 of 82 reported.

Twin tubal pregnancy may be bilateral, unilateral and even uniovular. For literature see Hardouin (27).

Repeated extra-uterine pregnancy is not infrequent. Brettauer and Peterson reported extra-uterine pregnancies occurring three times in the same patient (see Smith, 28). Normal intra-uterine pregnancy occurs often enough subsequently to justify allowing the unaffected tube to remain, if it appears normal to gross inspection at the time of operation.

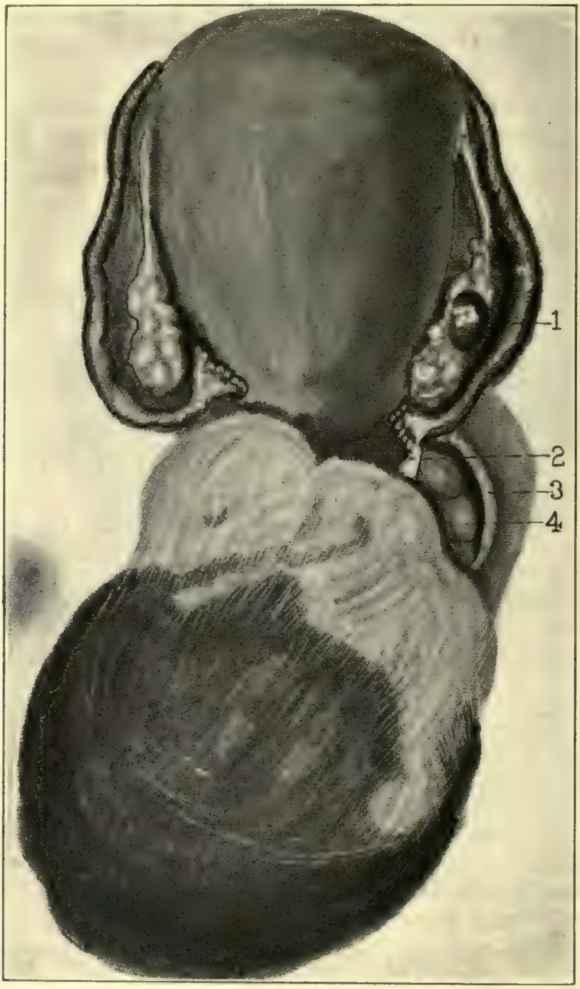

FIG. 305.—LITHOPEDION FORMATION (SECONDARY ABDOMINAL OR FIMBRIAL PREGNANCY.) 1. Right tube connected with the sac by an adhesion of the fibria ovarica. 2. Adhesion and ovarian fibria. 3. Sacro uterine fold. 4. Rectum. The lithopedion, still plainly showing its shape, lies within velamentous folds (remains of the amnion) upon the much-changed placenta.

Tubal pregnancy in the stump of a resected tube has been described by Vineberg (29) and others. Tubal pregnancy has occurred after vaginal hysterectomy, the point of entry being the tubal stump prolapsing through the vaginal vault.

Placenta Previa.—This anomalous insertion occurs about once in each 1000 pregnancies.

According to Doederlein (30, p. 992), in nearly six million labors it occurred 1 to 686, with a maternal mortality of 18.99 per cent and a fetal death rate of 49.32 per cent.

Multiparity favors it. The ovum may primarily insert low in the uterus (Jolly, 31), or, consequent to poor nutritive conditions, the placenta may be unduly spread out and remain velamentous, and thus encroach on the cervical region (Williams, 32).

Depending upon whether the placenta covers the dilated os completely (central), partially (lateral) or barely encroaches upon its edge (marginal) placenta previa is divided into three varieties.

The placenta, except for its site, may be normal. More often it is thinner and more extensive than the normally situated placenta.

The hemorrhage and consequent increase in fetal and maternal mortality is mainly of clinical interest.

As the large blood sinuses run through the poorly contractile cervical segment physiological hemostasis is incomplete. Air embolism is favored by this factor. Infection is more frequent, not only because of the more extensive operative interference required, but because microörganisms mount up from the vagina more early than to the usual fundal placental site.

Cervical Pregnancy.—This is a still more pronounced form of placenta previa. This variety is very rare. Rubin (33) was able to find only 7 authentic cases, to which he adds one.

To make this diagnosis Rubin demands that the main portion of the placenta be below the insertion of the uterine vessels, that cervical glands be present at the placental site, and that no fetal elements be found in the corpus uteri. In his case intraperitoneal hemorrhage occurred from rupture of the anterior uterine wall.

The conditions above described—extra-uterine pregnancy, placenta previa and cervical pregnancy—are pathological because of abnormality in the site of nidation. What follows deals with abnormalities and diseases of the decidua, amnion and chorion *per se*.

Decidua.—The older authors describe "endometritis deciduae," either diffuse or polypoid in character. The writer has never encountered such a condition either early or late in pregnancy.

An acute infection of *the decidua* occurs after attempts at criminal abortion. The decidua then shows marked leucocytic and round-cell infiltration.

Hydrorrhea gravidarum may be due to accumulation of fluid between the decidua vera and capsularis. More often the fluid is amniotic in origin, escaping from a small rent situated high up. The fetus may also escape

through the rent and develop extra-amniotically with resultant malformations (Meyer-Ruegg, 34).

Placenta accreta results when the spongy layer of the decidua is defective or atrophic (on uterine septa, over submucous myomata, in atrophy of the mucosa). The fetal trophoblast burrows deeply into the musculature and the placental villi are found attached to the muscle layer, without interposition of any mucosa. The placenta may remain inseparably adherent to its point of attachment.

Amnion.—The most important disturbance is due to the accumulation of too much amniotic fluid. *Hydramnios* is a quantity above 2 liters. As much as 30 liters have been noted. The causes differ in different cases—maternal edema, obstructions in the fetal cord, an excess secretion of fetal urine, disease of the amnion with reduction of its absorptive power, fetal disease (heptatitis, hydrops universalis) all have been blamed.

Acute hydramnios may be found in one sac of uniovular twins. The resultant hydramnios and anasarca (also heart and renal hypertrophy) may develop if the arteries of one placenta anastomose with the veins of the other, more fluid being thus pumped into the second circulation.

Oligohydramnios, or too scanty fluid, may produce adhesions to the fetus and malformations.

Intra-amniotic membranes are due to the organization of exudates or hemorrhages in the amniotic cavity. Self amputation of fetal members may result.

The Umbilical Cord.—The cord may vary in length from a few centimeters to two meters. Its normal length is 50 cm. Too short a cord may interfere with the descent of the child and may rupture during labor. (Fig. 306.)

The insertion of the cord into the placenta is usually excentric. Williams (l. c. 32, p. 645) found only 18 per cent central. In about 1 per cent a velamentous insertion (the vessels separating before they reach the placenta and coursing independently along the amnion) is noted. If the vessels cross over the internal os (vasa previa) they may rupture intra partum.

False knots of the cord are varicose dilations of the vessels. Varices may rupture, causing hematoma of the cord. True knots are usually loose, rarely they become tight during pregnancy or labor with resulting death of the fetus (Frank, 35) (Fig. 307). Torsion of the cord may cause fetal death; more often the twisting follows upon fetal death.

Rarely atrophy of an extremity results from continued constriction exerted by a loop of the cord. Monamniotic twins may die from intertwining and constriction of the cords.

Edema of the cord may be found fetalward from a true tight knot; it is also seen throughout the cord in hydrops fetus universalis.

Tumors of the cord are uncommon. Myxomata, myxo-sarcomata and teratomata have been described (for lit. see Williams, l. c. 32, p. 647). True

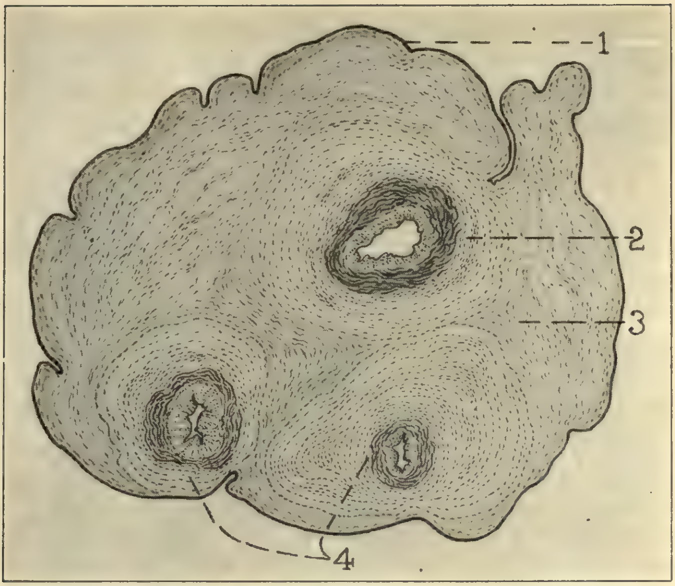

FIG. 306.—TRANSVERSE SECTION OF A NORMAL UMBILICAL CORD AT TERM. (×10.) 1. Amnion covering the cord. 2. Single umbilical vein. 3. Wharton's jelly. 4. The two umbilical arteries.

FIG. 307.—TIGHT KNOT OF THE CORD CAUSING FETAL DEATH. Note collapsed condition below the knot, engorgement above the obstruction. Fetal death occurred at term, 24 hours before the onset of labor.

cysts lined with epithelium are small, larger unlined cavities result from liquefaction of Wharton's jelly.

Syphilitic changes in the cord occur at the fetal end (spirochetes, endarteritis, leucocytic infiltration). See p. 209.

CHORION

The Fully Formed Placenta.—The gross changes noted are mainly those of shape, size and weight.

SHAPE.—Normally the placenta is discoid. Rarely it remains paper-thin, membranaceous and diffuse, from failure of the villi to atrophy, or *zonular* as in the carnivora. Incisures may produce a bipartate or tripartate afterbirth, an aperture produces a fenestrated placenta. Small accessory placental lobules developed on the membranes are known as succenturiate. A yellow whitish band extending around the fetal surface of the placenta beneath the amnion produces a marginate placenta. A centrally depressed placenta surrounded by an elevated margin from the edge of which the amnion extends is a placenta circumvallata.

Twin placentae may be separate, partly united, or fused. Usually two amniotic cavities exist, though monamniotic twins occur as the result of breaking down of the amniotic septa.

SIZE AND WEIGHT.—A full-term placenta is from 15 to 20 cm. in diameter and from 1.5 to 3 cm. in thickness. In syphilis, edema of the fetus, and in albuminuria, the relation of 1 to 6 (500 gms. to 3000 gms.) is disturbed and placentae are found which weigh as much as 2 to 2.5 kg. Such placentae are light pink and edematous, as if laked with water.

INFARCTS.—Whitish to yellowish areas of various shape and size (round, oval, wedge-shaped, from a few millimeters in diameter to areas occupying ⅛ or ¼ of the placenta) are of frequent occurrence, appearing on the fetal or maternal surface. They are firm and avascular, sometimes retracted below the general surface. Unless of large area and very numerous, infarcts are of no importance; if large they may lead to undernutrition and death of the fetus. Nephritis or syphilis are often found in cases of extensive infarction, but infarcts are not pathognomonic of any disease.

Microscopically, slow degeneration of the villi is noted, with fibrin filling out the intervillous space. Depending upon the stage at which the infarct is examined the villi appear first swollen, their vessels obliterated but the epithelial covering well preserved. Later the villi show as ill-defined shadows lacking all definition and cellular covering, amid fibrillar, hyaline or granular fibrin (Fig. 308).

The causes may be either an endarteritis of the fetal vessels, or a thrombosis in the intervillous space, probably due to destruction of the chorionepithelium, which then no longer prevents coagulation.

Calcification occurs in small areas, within the thrombotic fibrin of the intervillous space, and also within the stroma of degenerating villi.

For tuberculosis of the placenta see page 206.

For syphilis of the placenta see page 209.

TUMORS.—*Cysts* of the placenta are not infrequent. They may result from the partial absorptior of hemorrhages, from liquefaction of decidua

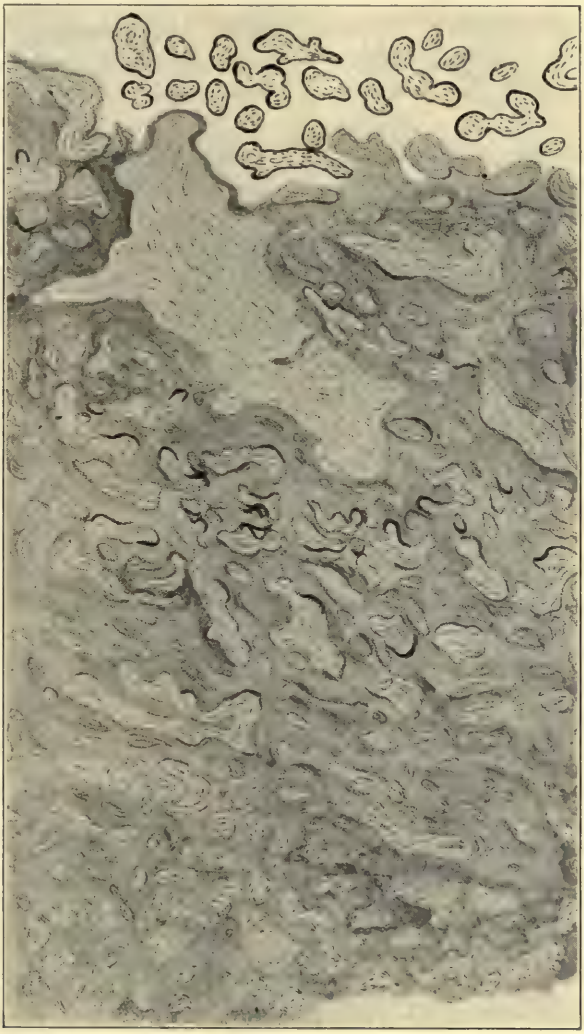

FIG. 308.—INFARCT OF THE PLACENTA: AT TERM. (Low power.) Above are normal villi and a free intervillous space. Toward the bottom the intervillous space is filled with formless débris in which lie more or less well preserved villi, some being mere " shadows."

adjacent to the placenta (and project into the amniotic cavity), liquefaction of infarcts or from areas of degenerated Langhans' cells. The cysts are from cherry to plum size and are lined with a whitish membrane. The contents may be clear or creamy fluid. The lining may contain one or more layers of trophoblastic cells or merely be composed of fibrin.

Solid tumors of the placenta are infrequent. Nebesky (36) collected 89 cases. All can be classed as capillary angiomata arising from the villi, although they have been reported as myxomas, angiomas, fibromas, and sarcomas, depending upon the amount and density of the fibrous tissue present. The growths are usually circumscribed, cherry to apple-sized tumors with a well-defined vascular pedicle. They may project above the surface or lie concealed within the placental tissue. Occasionally the tumors are multiple. Fetal death occurred in 35 to 40 per cent (Nebesky, l. c. 36).

Microscopically, innumerable endothelial-lined vascular channels lie amid a fibrous or edematous stroma. If the blood vessels are empty and collapsed, more solid-looking areas are noted, in which careful scrutiny alone will demonstrate the slitlike lumina.

Metastatic tumors of the placenta have been described. Walz (37) reported multiple metastases from a myxosarcoma of the leg; Senge (38), cancer metastases from a gastric tumor.

Early Chorion; Abortion.—Abortion is the expulsion of the products of conception before the period of viability (i.e., the 28th week) is reached. Before the 12th week the ovum is often expelled entire, including the decidua vera; between the 12th and 28th week the fetus is usually expelled first and the placenta and membranes follow.

Frequency.—According to Taussig (39) the ratio of abortions to confinements is as 1 is to 2.3. The writer (40), in 2000 unselected polyclinical gynecological cases, found that 721 had aborted at least once (of these 166 aborted twice, and 82 three or more times). The number of induced abortions is great.

Etiology.—One of the commonest causes of abortion early in pregnancy is death of the fetus from malformation (Mall, 41), and accidental causes (torsion of cord, etc.).

Very small fetuses are infiltrated with leucocytes and may be totally absorbed, often a stump of cord remaining. Older fetuses become *macerated*—fetus sanguinolentus (skin peels off in flakes, the surface appearing dull red, body swollen, skull soft, brain semifluid; blood-stained fluid in serous cavities, organs pulpy and no longer taking histological stains), *mummified,* and in the case of twins, one may be *compressed* or paper thin (*papyraceus*).

Other causes are infantile uterus, incarceration from retroflexion, and acute infectious diseases. In the later months multiple placental infarctions, premature placental detachment, and syphilis, produce fetal death and abortion.

Varieties.—In the first three months the products of conception are most often expelled as a blood or fleshy mole.

A *blood mole* is an elongated, brick-red mass containing a small amniotic cavity (with or without fetus) surrounded by lamellated fibrin and blood coagula deposited in layers. If the blood pigment has been absorbed,

a paler *fleshy mole* (Fig. 309) is formed. Calcification may produce a *stony* mole.

Microscopically, villi in various stages of degeneration are found in blood moles, often with the chorion epithelium in active proliferation (Fig. 310). After longer periods of retention the villi appear as pale shadows in a deeper staining detritus (Fig. 311).

Occasionally the decidua is expelled first and may then show no villi. It may be mistaken for the uterine cast of an ectopic pregnancy (Frank, 42), or for a dysmenorrhoic membrane. Sometimes, especially in curetted material, the villi will be few in number and hidden by voluminous

FIG. 309.—FLESHY MOLE RETAINED THIRTEEN MONTHS IN UTERO. Central amniotic cavity thick walls.

clot, requiring prolonged and careful search to find even one villus. (Figs. 312–313).

The leucocytic and round-celled infiltration of the decidua is most marked in infected, induced abortions and in abortions slowly expelled. It is secondary in most instances.

Hematom-mole or "subchorial tuberous hematoma of Breus" is a subvariety of early abortion in which rounded protuberances project into the amniotic cavity (Fig. 314). The thick mass is fleshy, the fetus is disproportionately small or absent and the villi show proliferation of their epi-

thelium (Fig. 315). The exact cause is unknown. For literature see Taussig (43).

In incomplete abortion not only is the decidua retained (this is physiological), but parts of the chorion and amnion may remain in the uterus for months. Irregular hemorrhages may result.

Small particles of trophoblast will serve to prolong the pregnancy reaction of the mucosa indefinitely. Decidual islands and chorionic wandering

FIG. 310.—VILLI IN EARLY ABORTION. (Medium power.) The large villus with well-marked Langhans' and syncytial layer, has a cell island at its apex. There are blood, fibrin, syncytial masses and small villi around the periphery.

cells will be found in the vicinity of retained villi. The uterus remains subinvoluted.

Large masses of chorion can be gradually encapsulated by concentric layers of fibrin and blood, forming polypoid tumors—*placental polypi.* These consist usually of well-preserved villi with proliferating chorion epithelium, fibrin, blood, and round-cell infiltration, embedded upon a thick

decidual layer of mucosa (Fig. 316). Retained portions of placenta at term may form identical tumors.

The mucosa after abortion, just as after labor at term, in the vast

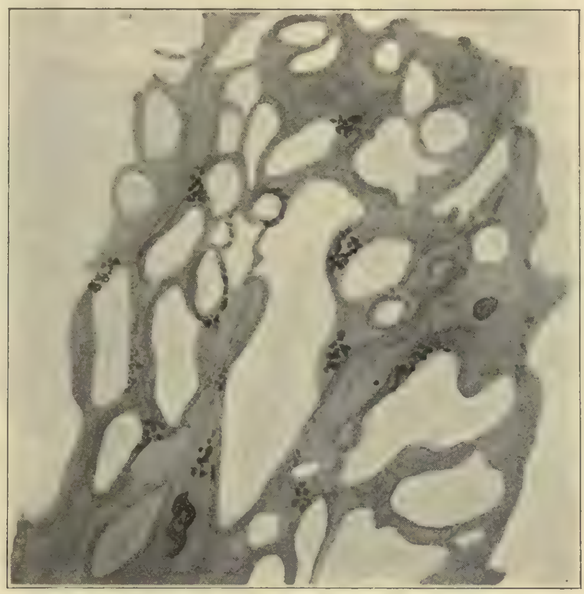

FIG. 311.—FLESHY MOLE, MEDIUM POWER OF FIG. 309. The light portions are the "shadows" of villi. Fibrin is stained dark, with small areas of calcification showing as black areas.

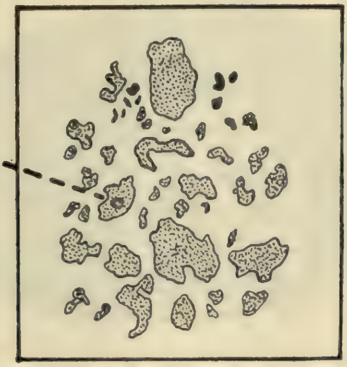

FIG. 312.—SLIDE FROM CURETTINGS OF A BLEEDING PATIENT. (×2.) Slight enlargement of the paraffin section of the curettings. All the material proved to be endometrium except that within the small rimmed circle.

majority of cases, rapidly returns to the resting stage preparatory to again undergoing the regular cyclical changes (see p. 95).

If the ovum dies but does not produce a strong foreign body stimulus, or the uterus is inert, or both, expulsion does not occur. In the early

months this is called *missed abortion,* after the 28th week, *missed labor.* Retention may continue for years or months and the enlargement be ascribed to uterine tumor.

Chorion; Neoplastic Changes.—The reader is advised to refresh his memory on the details of nidation, and the histology of the chorionic villus

FIG. 313.—MEDIUM POWER OF FIG. 312. AREA WITHIN THE CIRCLE ENLARGED. Two villi found in the rimmed circle; no other to be found in the rest of the material. 1. Fibrin. 2. Degenerating villus. 3. Red blood cells. 4. Cell islet (chorionic) with two decidual cells below.

FIG. 314.—BREUS HEMATOM-MOLE LAID OPEN. (X1.) Above the thick, fleshy wall. Centrally and below, the amniotic cavity bulged out by subchorial hematomata.

(p. 87) in order that he may be able to follow the gradual transition from normal pregnancy to hydatid mole and chorionepithelioma.

Normal pregnancy is a symbiosis of a parasite (fetus) and host (mother). Probably the decidua and the fibrin layer (Nitabusch's) interpose a barrier to the erosive action of the trophoblast. The fragments of

villi which are normally carried off into the maternal circulation (see Fig. 298, p. 448) are disposed of by lytic action of the body fluids. A disturbance of these defensive factors and an increase in cellular activity of the trophoblast would account for successful invasion of the maternal organism.

Hydatid Mole.—This is of frequent occurrence. Storch (44), in a series of early, unselected abortive ova, found that three-quarters showed hydatid changes. Clinically noticeable moles occur according to Findley (45) in from 3: 1000 to 1: 728 pregnancies, repeated molar pregnancy was noted 7 times in 500 cases of hydatid.

FIG. 315.—BREUS MOLE. (Low power.) Above and toward right is degenerated amnion. Throughout are blood clots, degenerated villi and chorionic wandering cells.

Between fully developed hydatid mole and the normal ovum a number of transition stages exist. Healthy children have been born, a small part of whose placenta had undergone hydatidiform changes. Twins, the one normal, the other represented by an hydatid, have repeatedly been observed. These cases demonstrate that no fundamental differences exist between hydatid and the normal products of conception. Moreover the hydatid produces certain changes usually associated with pregnancy, of which the most striking are decidua formation in the uterus and enlargement of the breasts. Even if untreated, the uterus which harbors a mole may expel its contents, in the third to fifth month, like a uterus at term. Complications ordinarily seen in pregnancy—hyperemesis, toxemia, eclampsia, may occur.

The age incidence, according to Findley (l. c. 45) is as follows:

Below 15 years..... 3	35 to 45 years...... 84
15 to 25 years......111	45 to 50 years...... 36
25 to 35 years......143	50 to 55 years...... 17

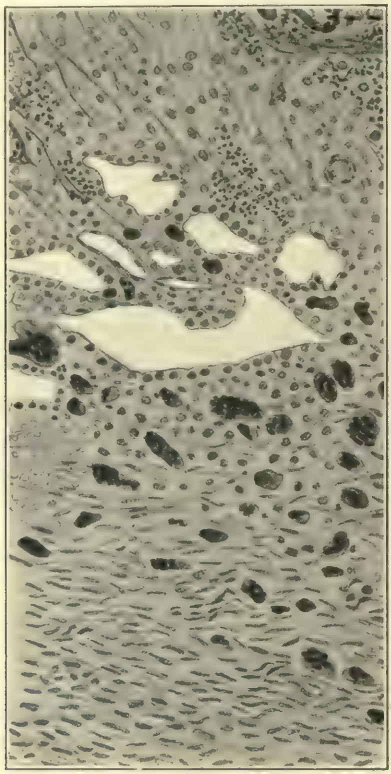

FIG. 316.—PLACENTAL POLYP: BENIGN. (High power.) At the extreme upper right, part of a villus is shown. In the middle, is the spongy layer of the decidua with gland lumina showing as open spaces. Below this area are numerous chorionic wandering cells, which resemble dark giant cells, and penetrate the uterine muscle at the bottom of the section.

MACROSCOPIC APPEARANCE.—This varies according to the extent of the involvement and the time of its incidence. A few minute vesicles may be found in a full-term placenta. In other instances one twin may be normal, the other represented by a molar pregnancy. If the process begins before the second month no trace of fetus or amniotic cavity will be found.

A typical hydatid mole consists of a mass of translucent, grapelike vesicles attached to one another by thin, threadlike stalks. The vesicles vary from pinpoint size to hazelnut size. If expelled from the uterus they are loosely cemented together by fragments of decidua and blood clot. In the uterus they may be diffusely attached to all parts of the interior or limited to a site corresponding to the placental area.

Irregular, profuse hemorrhages, rapid growth of the uterus disproportionate to the duration of pregnancy, and frequent occurrence of edema and albuminuria characterize the clinical picture. Expulsion usually takes place between the third and fifth month of gestation.

MICROSCOPIC APPEARANCE.—The ordinary hydatid shows the groundwork of the villus swollen, hydropic, and often containing either calcareous

FIG. 317.—HYDATID MOLE (Photomicrograph.) (Low power.) Hydropic stroma, proliferating trophoblast are shown.

or hyaline areas. Macroscopically this accounts for the translucent grape-like bodies. Microscopically, the edematous, semifluid stroma contains occasional connective tissue cells of the embryonal type, fetal blood vessels in very small number and the above mentioned hyaline or calcareous areas. The villous covering may be normal, but more often a great increase in proliferation of the Langhans' cells and more numerous, more irregularly

distributed syncytial buds, and, in general, a more luxuriant and atypical growth of the entire ectoderm is noted. All varieties of transition between the normal distribution of the trophoblast and excessive and widely infiltrating proliferations are on record (see Figs. 317 and 318).

VARIATIONS.—The hydatid mole shows a similar diversity in its clinical course; some proving benign, others highly malignant, though the microscopical findings afford no guide to this. The great majority of hydatids are benign, some, however, invade the uterine wall, others produce metastases (Pick, 46) (Fig. 319), while a small number are truly malignant and cause death by general dissemination (Salowij and Krzyszkowski,

FIG. 318.—HYDATID MOLE. (Medium power.) Shows hydropic stroma of villus with calcified center. Syncytial buds (dark) with multiple nuclei lie peripherally. Langhans' cells (clear, with well-marked cell boundaries) are in close relation to the syncytium.

47). This last variety is to be distinguished from chorionepithelioma in those parts only, both at the primary site and in the metastases, in which a direct connection between the invading trophoblast and the hydropic villus stroma can be demonstrated. In sections, for instance, in which no part of the stroma happens to be included, the picture is that of a typical chorionepithelioma malignum.

Perforation of the uterus has been reported with intraperitoneal hemorrhage. Hydatid degeneration of a tubal pregnancy has occurred (Matwejew and Sykow, 48).

COURSE.—Death from hemorrhage (3 per cent), perforation of uterus 2 per cent), infection (5 per cent) and other causes occur (total 10 per cent, Findley, l. c. 45). Findley, in 500 cases, found 157, or 31.4 per cent followed by chorionepithelioma. This percentage is disproportionately high. Teacher (49) believes even 5 per cent too high an estimate.

FIG. 319.—VAGINAL METASTASIS OF A BENIGN HYDATID MOLE. (Photomicrograph.) (Case of Prof. L. Pick of Berlin.) Above and to the left a hydatid villus is seen breaking through the squamous epithelium of the vagina.

Chorionepithelioma.—Direct transitions from hydatid mole to malignant chorionepithelioma are numerous. In such tumors the origin of voluminous, diffusely infiltrating trophoblastic cells which invade the host and produce distant metastases can readily be traced from the villus (Fig.

320). A vast literature has arisen, much of which is casuistic and, even more, theoretical.

FREQUENCY.—Vineberg (50) was able to collect 533 cases in 1917. Doubtless to-day many cases are not published.

FIG. 320.—TYPICAL CHORIONEPITHELIOMA OF THE UTERUS SHOWING CHORIONIC VILLUS. Photomicrograph. (Medium power.) (Case of Prof. L. Pick of Berlin.)

The following table shows the conditions anteceding the disease:

	Teacher 188 Cases	Pollosson & Violet 455 Cases	Hitschmann & Christopholletti 240 Cases
Hydatid	73 (36.6%)	203 (45%)	116 (48%)
Abortion	59 (31%)	135 (30%)	73 (30.4%)
Pregn. at term	49 (28%)	99 (21%)	51 (21%)
Extra-uterine..	7 (4.4%)	12 (2.5%)	

No reliable statistics showing the frequency compared to other genital neoplasms is available.

AGE.—Teacher (l. c. 49, p. 579), in 189 cases, found the youngest 17 years old, the oldest 55; the average age 33 years. Sixty-seven per cent occurred between 20 to 40 years.

FERTILITY.—This appears to have a direct bearing on the incidence, a rise being noticed with the frequency of births. According to Teacher:

First pregnancy	4.77%
After first pregnancy	15.37%
After second and third pregnancy	28.24%
After five or more pregnancies	37.8%

LATENT PERIOD.—Rarely, metastases have been noted during pregnancy (Pick, l. c. 46), three days before expulsion of an hydatid; Walthard (51), during eighth month of normal pregnancy). In a larger number, tumor formation (either local or metastatic) appeared in from 1 week to 4 months after labor or abortion. In a smaller number long latency has been noted, up to 13 years (Polano, 53).

MACROSCOPIC APPEARANCE.—The uterine tumors, which are the most frequent, appear early either as irregular, elevated, submucous nodules of blue-black, hemorrhagic color or like ragged thrombotic placental remnants high in the corpus. Later, voluminous hemorrhagic tumor masses may fill the uterine cavity, bleeding alarmingly at the slightest instrumental interference, or the mass may be expelled, a ragged ulcer remaining.

The uterus is enlarged and usually soft. Other nodules may be found interstitially and subperitoneally.

Sometimes no connection with a previous placental site can be discovered—*"ectopic"* chorionepithelioma (Findley, 54). Sternberg (55) reported a tumor of the portio vaginalis, Lecène (56) of the broad ligament, and the writer (23) one intraperitoneally over the point of division of the internal iliac artery.

Tumors may be largely intravenous, appearing as variegated thrombotic veins of the broad ligament. Vaginal tumors, in particular, look like hematomata or thrombi. The main portion of such masses are coagula, active tumor tissue being limited to the periphery.

Risel (57) in 1914 collected 22 cases of chorionepithelioma of the *Fallopian Tube*. The tumor early resembles ectopic pregnancy, from which it may arise. Later, infiltrating, friable, hemorrhagic tumors develop. The percentage of recurrence is unduly high (85 per cent). *Ovarian* chorionepitheliomata may result from uterine, tubal or ovarian pregnancy (from teratomata, see p. 426). *Vaginal* growths are rarely primary(i.e., ectopic) usually they are metastases of uterine tumors.

MICROSCOPIC APPEARANCE.—Marchand's (58) description still applies. He divides the growths into two forms, the typical and the atypical.

The typical form closely imitates the trophoblast of the earlier months of pregnancy, showing a tissue composed of Langhans' cells, intermixed or traversed by large syncytial masses, containing also chorionic wandering cells, and hemorrhagic and necrotic areas. In favorable sections erosion of maternal blood vessels, Langhans' cells in the lumen of small veins, and, in general, where the invasion of the uterine muscle can be traced, an appearance, resembling to some degree the proliferation of a carcinoma can be observed (see Figs. 321 and 322). Nearly everywhere the intimate relation of the individual cells to fibrin is plainly shown. Nowhere is there

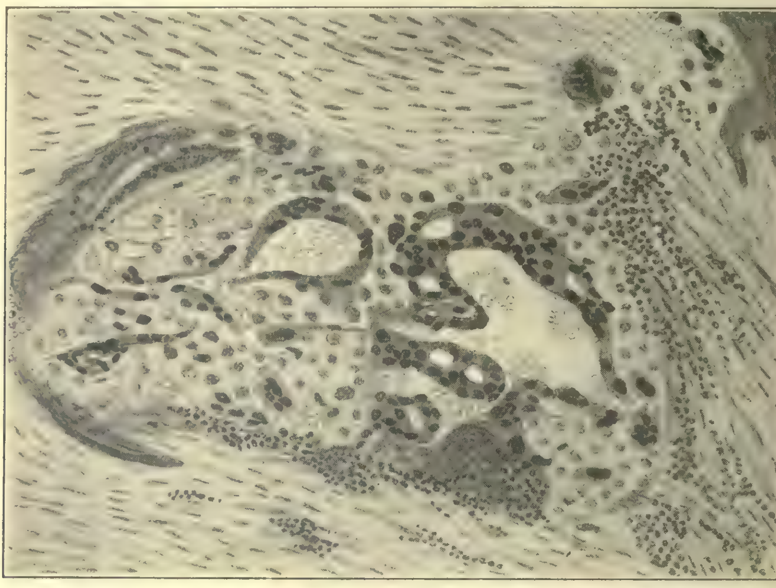

FIG. 321.—TYPICAL CHORIONEPITHELIOMA OF THE UTERUS. (Medium power.) Within the uterine musculature is a hemorrhagic area containing syncytium, Langhans' cells, fibrin and red blood cells. Round-cell infiltration occurs peripherally.

any indication of a new formed connective tissue or vessels, such as is seen in other neoplasms.

In the atypical form the Langhans' cells are less numerous, large syncytia are infrequent or absent, and a more diffuse invasion of the maternal structures, by cells of the type of chorionic wandering cells, large mononuclear or polynuclear, deeply staining cells giving the impression of a sarcomatous tissue, are noted. These cells show a marked tendency to attack the smaller blood vessels, and are characterized by great variations in size, shape and appearance of the nuclei. (See Fig. 323.) Intermediate forms, in which a preponderance of either of these types may appear, are not infrequent. (See Fig. 324.)

Some authors have described purely syncytial tumors but Marchand

believes it likely that, at least in some portion of these growths, Langhans' cells can be discovered.

Ewing (59) has attempted to divide chorionepithelioma into three groups (choriocarcinoma, chorio-adenoma and syncytioma) with a definite

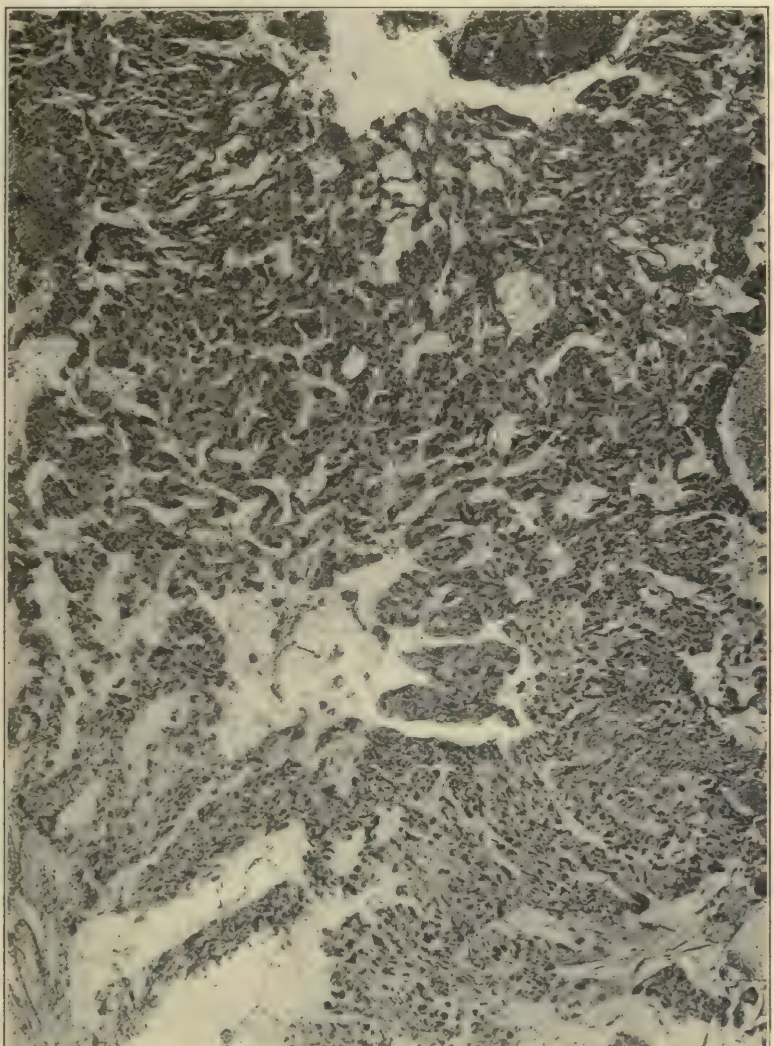

FIG. 322.—TYPICAL CHORIONEPITHELIOMA. (Photomicrograph.) (Medium power.)

potential malignancy for each. His classification has not met with general acceptance. Geist (60) in a recent paper, based upon an inadequately small number of cases, accepts Ewing's criteria. As with all previous attempts, however laudable, it must be emphasized that *histological criteria are unreliable* (for lit. see Ewing, l. c. 59, p. 388).

Metastases are frequent, dissemination occurring through the blood stream. Where no primary tumor referable to the placental site is discoverable the growth (then known as an "ectopic" chorionepithelioma) is presumably derived from a placenta which was entirely expelled. In Walthard's case (l. c. 51) the term placenta was minutely examined and found normal.

Metastases are most frequent in the lungs (apex and base) (Fig. 325), next in the vagina, vulva, liver. The nodules appear as hemorrhagic or thrombotic areas. Usually the morphology is identical with that of the primary growth although variations are noted. Rarely villi are found.

FIG. 323.—ATYPICAL CHORIONEPITHELIOMA UTERI. (Medium power.) No Langhans' cells occur, the tumor consisting mainly of chorionic wandering cells, red blood cells and fibrin.

Regression is evidenced by a strong connective tissue reaction of the invaded organ, and encapsulation of the tumor cells by dense thrombi.

Rarer location of metastatic growths are the adnexa, broad ligaments, the urinary organs, brain, spinal cord, gastro-intestinal tract, heart, thyroid, pancreas, subcutaneous tissue.

REGRESSION.—Recovery *after curettage* has been reported (v. Velits, 61, collection of eight cases).

Recovery *after incomplete operation* (hysterectomy, impossibility to resect thrombosed veins, etc.), Ewing (l. c. 59) mentions seven cases.

Rockafellow's case (62) in which the uterine, and three successive

labial tumors were removed and the fourth labial recurrence spontaneously regressed is the most striking instance.

FIG. 324.—ATYPICAL CHORIONEPITHELIOMA UTERI. (Photomicrograph.) (Medium power.) Diffuse invasion of the muscle by sarcomalike cells characterizes this form and accounts for the diagnosis of "deciduoma."

Recovery after occurrence of *vaginal metastases.* Schmauch (63) collected 13 cases. Supposedly pulmonary metastases (cough, hemoptysis) have also been recovered from (Fleischmann, 64).

Regression, therefore, appears more frequent in chorionepithelioma than in any other type of malignant tumor. Marked differences in malignancy are also characteristic. However, a certain regularity is manifested, depending upon the source.

Cures.—According to Pollosson and Violet (65): After hydatid mole recoveries, 68 per cent; after abortion or delivery recoveries, 58 per cent;

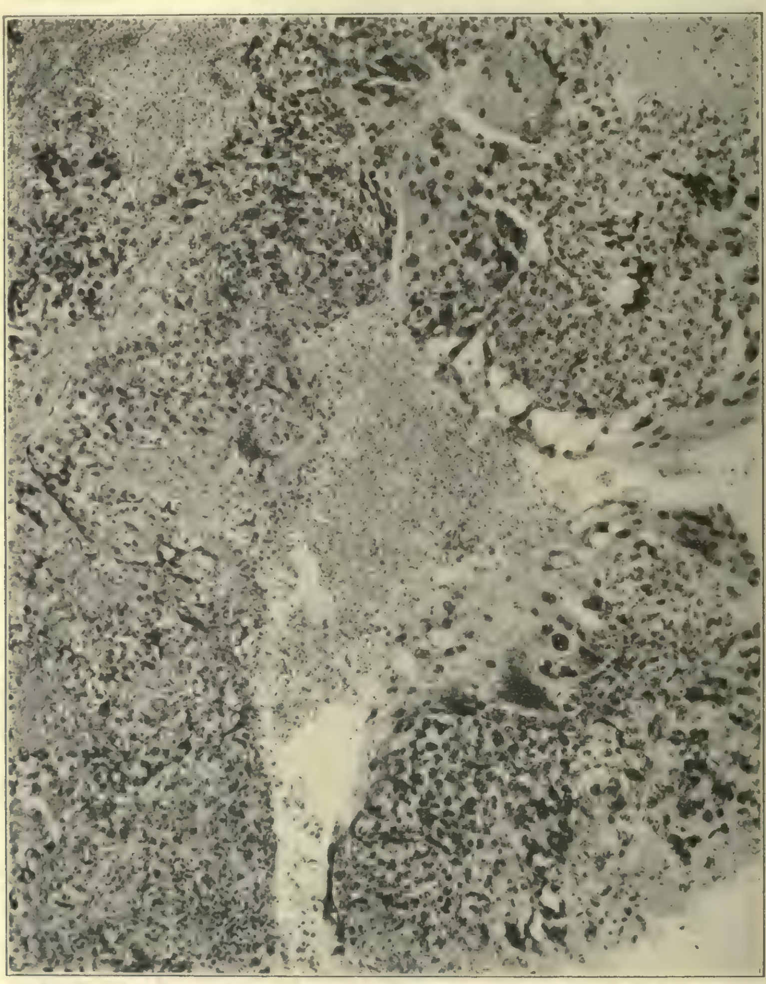

FIG. 325.—LUNG METASTASIS OF ATYPICAL CHORIONEPITHELIOMA. (Photomicrograph.) (Medium power.)

after tubal pregnancy recoveries, 33 per cent, although Cope and Kettle (Proc. Royal Soc. Med. (O. & G. Sect.) 1913, VI, 11, 247) found only two recoveries in 14 cases.

Teacher (l. c. 49, p. 590), in 100 operated cases, found that 37 died. Of the 63 who survived, 32 were well six months later, 24 one year, and 13 two years later. Recurrence usually takes place within one year.

Diagnosis.—The clinical history is of importance. Molar pregnancy is always suspicious. Vineberg's suggestion (l. c. 50) to perform vaginal hysterotomy is valuable. Palpation in the uterine wall of an elevated, firm nodule with a craterlike excavation is pathognomonic.

The suggestions given by the writer in 1906 (66) in regard to the course to be pursued still apply.

1. A curettage should regularly be performed after the removal of an hydatid mole, and the scrapings be subjected to careful examination. If

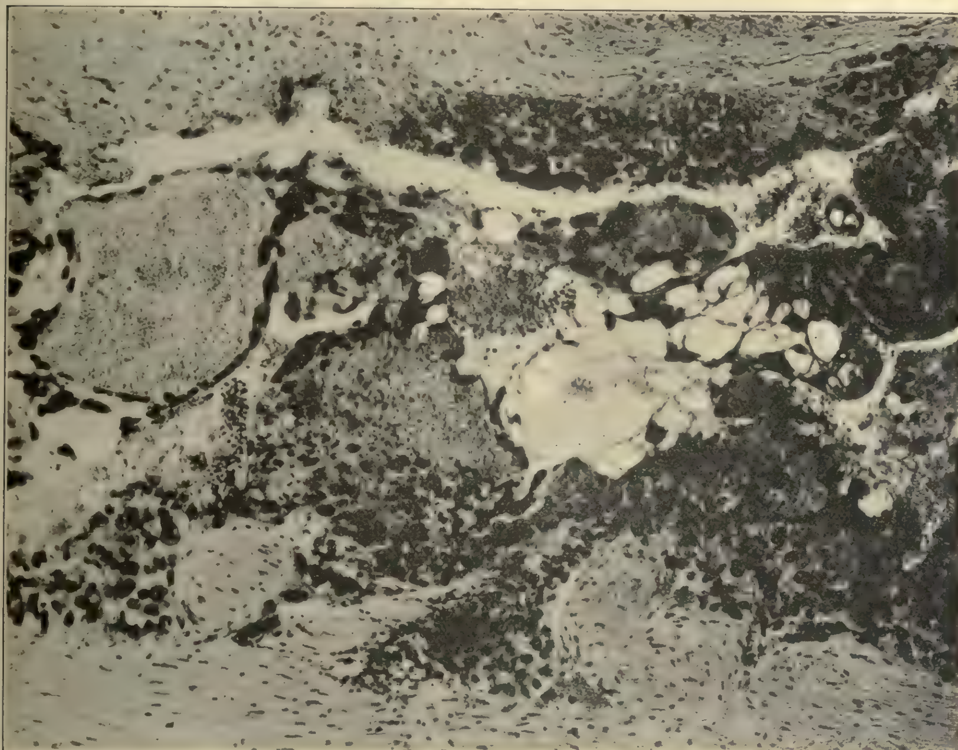

Fig. 326.—Chorionepithelioma of the testis. (Photomicrograph.) (High power.) This tumor shows the exact similarity in morphology of the teratomatous and gestational types. Such tumors occur in the testes of young males and rapidly spread into the abdomen.

subsequently, hemorrhage develop, and masses of fetal tissue are obtained from the uterus which we positively know to have been emptied before, hysterectomy is indicated unless the youth or nulliparity of the patient induce the physician to extend the time of observation; if the muscle is infiltrated with many fetal elements at this late date the same course is advisable.

2. Persistent postabortive hemorrhages should not be indefinitely treated by palliative measures. After two or three weeks' time has elapsed regenerative processes should be well under way and a curetting for diag-

nostic purposes ought to be done. Persistence of isolated fetal elements is not pathological. If at a later date renewed hemorrhages induce the medical attendant to perform a second curettage, and erosion of the uterine wall, the presence of fungoid placental masses, or an increase of fetal elements in the curettings appear, hysterectomy must be seriously considered.

3. In rare instances placental polypi may precede chorionepithelioma. The polyp should be examined, its base in the mucosa carefully studied and the depth of the infiltration at this spot observed. Should renewed bleeding occur and the second curettings show many fetal elements the case is very suspicious. It will be noted that early, careful and conscientious emptying of the uterine cavity and microscopic examination of its contents will be of the greatest assistance in making a diagnosis at some later date, should symptoms persist or recur. For, if we are certain that the uterus was thoroughly emptied, the findings of active fetal tissues, after a reasonable interval, is a sure proof of a pathological, and almost always of a malignant process.

4. Even if vaginal metastases and considerable involvement of pelvic structures have occurred all hope need not be abandoned. Partial removal of diseased tissues has, in several cases, sufficed to cure permanently supposedly inoperable conditions.

Puerperal Infection.—Puerperal infections result from bacterial invasion of the genital tract. The invasion may take place before, during, or after abortion or labor. The numerous bruises, lacerations, denudations and injuries which result during parturition, afford innumerable points of entry. Infection would result in every instance if the defensive mechanisms (drainage, bactericidal body fluids, leucocytic wall, etc.) were not potent, and if virulent bacteria were always present.

Of the bacteria found, the most regularly present are streptococci, staphylococci, colon bacilli, gonococci. Rarely pneumococcus, typhoid, diphtheria and gas bacillus and various anaërobes are isolated.

In 324 febrile cases Williams (l. c. 32, p. 935) isolated the following bacteria from the uterus during the puerperium.

Streptococcus (5 anaërobic)	93
Staphylococcus (5 albus, 5 aureus)	10
Bacillus coli communis	21
Gonococcus	33
Bacillus aërogenes capsulatus	3
Unidentified (22 anaërobes)	28
Diphtheria	1
Typhoid	1
Cultures, negative, bacteria on cover slips	63
Sterile	68
Contaminated	2

Bacteriological tests give little or no indication of the virulence of bacteria. Usually the hemolytic streptococcus longus is the most virulent, but the s. viridans and mucosus may produce violent and fatal infections, and these may also follow introduction of the anaërobic streptococcus. At other times any of these forms may be present as harmless saprophytes. For literature see Williams (l. c. 32, pp. 930 and 945).

Before labor, streptococci are found on the vulva and in the vagina in from 5 to 75 per cent of cases, depending upon the cleanliness of the patient. Ahlfeld (67) concluded that *auto-infection* plays a large rôle in puerperal fever. The writer, however, agrees with Williams (l. c. 32, p. 951) that "serious streptococcic infection should always be regarded as evidence of external infection." Coitus, entrance of bathwater, self examination by the patient, examinations by the accoucheur, etc., introduce the germs.

Frequency.—Since the introduction of antisepsis and asepsis the mortality from puerperal infection has fallen to 0.1 of one per cent in well conducted maternities. *In private practice, on the other hand, the mortality still remains frightfully high.* Meigs (68), for 1900 to 1910, found a mortality of 6.5 per hundred thousand, which means over 4000 maternal deaths each year in the registration area (three-quarters of the U. S.). In women of 15 to 45 years of age childbearing is the second greatest cause of death (Davis, 69).

Types.—The lesions of puerperal infection depend upon many factors, among which the time of entry, the point of entry, the degree of injury present, the virulence of the bacteria, the defensive mechanism of the patient's body and the method of treatment play a rôle.

Two main varieties are encountered—a local, well defined and limited, mainly surface infection (saprophytic) and a diffuse, penetrating, advancing and systemic form (septic).

1. In so-called sapremic infection, which, however, may be due not only to colon bacilli, etc., but also to pyogenic organisms of low virulence, bacterial growth is limited to the necrotic tissues (surface of decidua, membranes, and placental fragments remaining after abortion and labor) producing a *putrid endometritis* (and ulcers of cervix, vagina or vulva). The affected areas are covered by a soft, green-gray, foul-smelling coating. Beneath this a demarcation area composed of a dense leucocytic wall forms, and the necrotic tissue is eventually cast off, leaving a clean ulcer (Fig. 327). Symptoms are mainly due to absorption of toxins. Rarely the infection is marked by gas production (colon bacillus, bac. aërogenes capsulatus), *tympany* of the uterus resulting. Still more infrequently the uterine limits are passed and a general gas gangrene of the cellular tissues and abdomen results.

2. In the septic types of infection, dissemination may occur through the *blood channels,* producing a general bacteremia (bacteria circulating and multiplying in the blood) with no or very slight local lesions.

A thrombophlebitic extension is less foudroyant, though often fatal.

Here a continuous infective venous thrombosis spreads in the channels of the pelvis, lower extremities and abdomen, or the local thrombotic process may be overshadowed by the multiple foci resulting from infective emboli carried to distant parts and there producing lesions (pyemia, lung abscess, panophthalmitis, perinephritic abscess, etc.). Not infrequently both subvarieties coexist. *Phlegmasia alba dolens* (or milkleg) is an avirulent form of thrombophlebitis of the saphenous or femoral vein. Puerperal *gangrene* of the lower extremities is a rare sequel of thrombosis (Wormser, 70).

In the less hyperacute cases the injuries in the lower birth canal, the entire interior of the uterus or only the placental site are covered with a dirty, yellowish-gray, fibrinous membrane. If no contaminating putre-

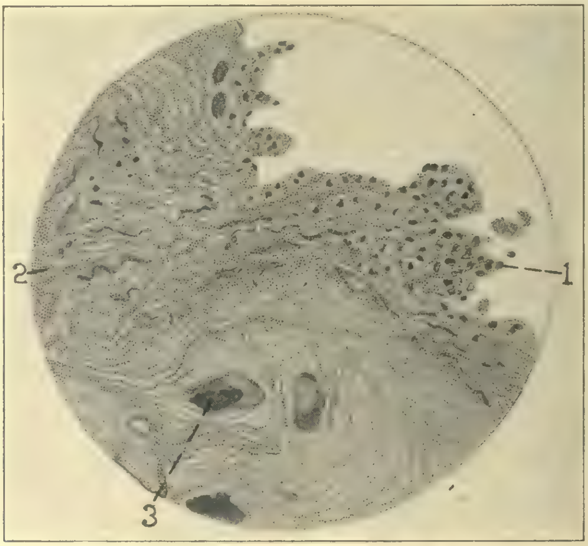

FIG. 327.—SEPTIC ABORTION, THIRD MONTH. SECTION FROM UTERINE WALL. (Low power.) 1. Necrotic decidua remaining after separation of the ovum. 2. Round cell and leucocytic wall. 3. Small thrombosed vessels in uterine wall.

factive bacteria are present the scant saneous discharge is odorless. Such *septic endometritis* may end in resolution, or local abscesses form in the uterus (see p. 183); large areas may necrose (metritis dissecans, p. 183) or infection may extend to the serous coat of the uterus, producing a septic perimetritis and peritonitis. (For details see Uterus, Chapter VII, p. 182).

In clear-cut septic types the leucocytic wall is not well developed. Bacteria are found in apparently healthy portions of the musculature, and especially in the thrombosed vessels (Fig. 328).

Extension from local ulcers in the vulva, vagina, cervix or uterine body may take place through the *lymph spaces* or *lymph channels*. Enlarged, beaded, yellowish-white lymph strands may be demonstrated, surrounded by areas of edema, infiltration or abscess in the paravaginal, paracervical,

parametrial and even retroperitoneal regions. Extension from uterus to tubes and ovaries are commonest by this route (see Chapter VII, p. 182).

Puerperal peritonitis is regularly of lymphatic origin. It is usually streptococcic, severe, of rapid spread, and quickly fatal. There may be a coincident pleurisy and pericarditis.

FIG. 328.—SEPTIC FATAL THROMBOPHLEBITIS, FIFTH MONTH. (Low power.) 1. Layer of necrotic fibrin lining the interior of the uterus. 2. Remains of the turgescent mucosa, each of its vessels dilated and thrombosed. 3. Large thrombosed veins in the uterine muscle. 4. Peritoneal surface of the uterus.

Combinations of thrombophlebitic and lymphatic forms are of frequent occurrence (Figs. 329–330). Bacteremias are often unaccompanied by demonstrable local lesions. Bacteria may be found in the blood immediately after instrumentation (curettage) or after a chill, and may then disappear

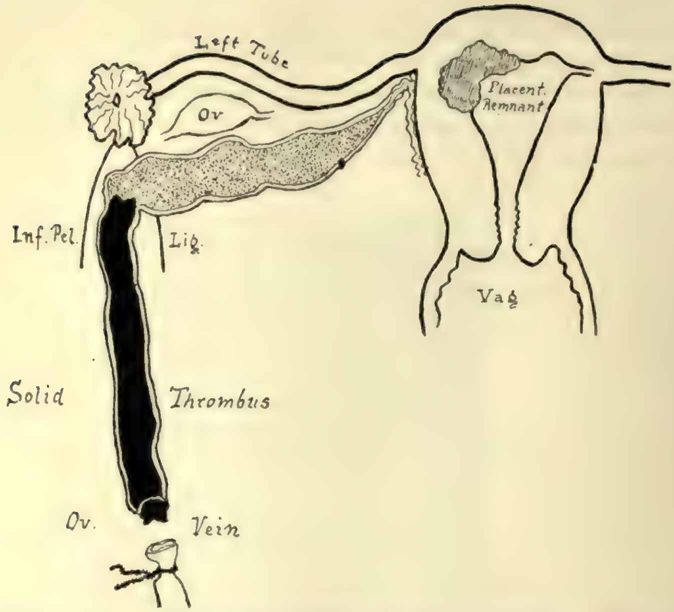

FIG. 329.—CASE OF THROMBOPHLEBITIS SHOWING MODE OF EXTENSION. (Operative findings.) Note the placental site, purulent thrombus in the ovarian vein and a solid thrombus above this. At the extreme bottom is the proximal part of the ovarian vein.

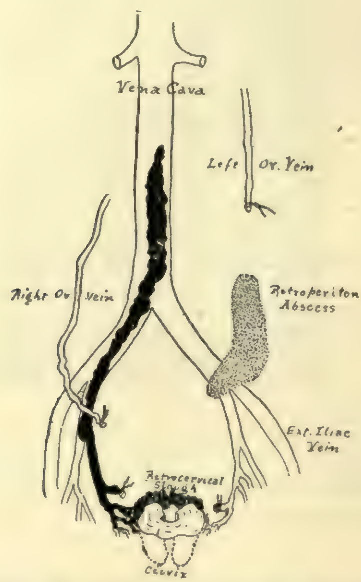

FIG. 330.—AUTOPSY ON PATIENT OF FIG. 329. Shows the thrombosis extending into the vena cava (venous infection) and also a retroperitoneal abscess on opposite side (lymphangitic infection).

in the course of a few hours. Endocardial lesions, miliary aneurisms and petechiae appear in the course of bacteremias.

The frequency of occurrence of the different types is difficult to estimate. In cases which recover no classification is possible.

The following statistics compiled from the reports of Grossmann, Trendelenburg, Faix, Opitz, Seegert, Lenhartz and Brettauer show that:

Of 966 severe puerperal infections, 461, or 47.5 per cent, died.

Of 256 fatal cases, 151, or 59 per cent, showed pure thrombophlebitis.

Of 226 fatal cases, 32, or 14 per cent, showed thrombophlebitis combined with lymphangitis.

Of 93 fatal cases, 63, or 67 per cent, showed bilateral pelvic thrombosis.

Of 93 fatal cases, 30, or 33 per cent, showed unilateral pelvic thrombosis.

Of 141 fatal cases, 37, or 26 per cent, showed multiple pelvic thrombi (uterine, ovarian, pampiniform, iliac).

Of 141 fatal cases, 12, or 8.5 per cent, showed cava thrombosis.

Of 141 fatal cases, 53, or 37.5 per cent, showed ovarian vein thrombosis.

Of 141 fatal cases, 34, or 24 per cent, showed uterine vein thrombosis.

Of 141 fatal cases, 3, or 2 per cent, showed femoral vein thrombosis.

Of 141 fatal cases, 2, or 1.5 per cent, showed iliac vein thrombosis.

Of 94 fatal cases, 70, or 74.5 per cent, showed pulmonary abscesses.

Of 60 fatal cases, 14, or 23 per cent, showed peritonitis.

The above statistics show why anatomical diagnosis *in vivo* is largely guess work. Combinations of different types, predominance of certain symptom groups, inaccessibility of lesions, account for differences in results and outcome.

A large number of those affected escape with their lives. Of infected criminal abortions less than 1 in 20 die. The survivors may show permanent parametrial, peritoneal and adnexal lesions. The same applies to non-fatal cases of puerperal infection subsequent to spontaneous labor.

TOXEMIAS OF PREGNANCY

Toxemia, Eclampsia, Acute Yellow Atrophy of the Liver.—In pregnancy the maternal organism is forced to perform a double task—to attend to the anabolic and katabolic metabolism of its own plus that of the fetus. If any insufficiency of the cardiac, renal, or pulmonary systems preëxist, symptoms may develop. But even previously healthy women may be unable to support the additional strain. Symptoms may take the form of albuminuria, toxic vomiting, eclampsia or acute yellow atrophy of the liver.

The albuminuria of pregnancy is an acute nephritic process implanted in many cases on a preëxisting mild, or a latent nephritis. Albuminuria and retinitic hemorrhages are characteristic.

The toxic vomiting of pregnancy is an acute acidosis in which profound liver changes are produced by the resulting inanition (central liver necroses).

Eclampsia is a toxemia occurring during pregnancy (25 per cent), labor (50 per cent) and the puerperium (25 per cent), characterized by convulsions, coma and death. Cases without convulsions likewise occur. The disease is noted in 1 to 500 or 600 pregnancies, primiparae forming 60 per cent. The maternal mortality is 20 to 25 per cent, the fetal deaths from 30 to 50 per cent. Eclampsia has been noted in hydatid and in tubal pregnancies and after death of the fetus.

The supposed causes are innumerable. For literature see Williams (l. c. 32, p. 568). The only certain fact is that some circulating poison produces severe changes most marked in the liver, changes which are produced also by phosphorus, chloroform and bacterial poisons (Frank and Heimann, 71).

The autopsy findings are:

The liver in eclampsia shows the most regular and typical changes. Grossly, a fatty appearance with hemorrhages varying from pin-point size to large foci, is noted. On microscopical examination necrotic areas are distinguished, marked by thrombi within the smaller, interlobular portal vessels. The necrotic areas, which are usually central, consist of more or less necrotic liver cells, the better preserved ones loaded with fat, the dead cells represented by formless masses. The boundaries of the diseased foci may be hemorrhagic or anemic, depending largely upon accidental conditions of circulation due to the thrombosis.

The kidneys, almost without exception, show cloudy swelling and acute fatty degeneration. Minute thrombi in the glomeruli and smaller artéries and veins are common. Dilatation of one or both ureters is not unusual, but this change is noted with almost equal frequency in normal pregnancy.

The convolutions of the brain are flattened and edematous. Minute or larger hemorrhages may be found; and some of these may be large enough to account for symptoms during life. The brain as a whole may be congested or anemic.

The lungs are almost always congested and edematous; probably due to terminal conditions, referable to the mode of death. Thrombi and emboli consisting of fibrin, liver, placental fat or bone marrow cells are noted. These emboli, however, are also seen in other diseases and in normal pregnancy (Pels-Leusden (72)). Their greater number in eclampsia is accounted for by the severe exertion resulting from the general convulsions.

The heart shows marked fatty changes and punctate hemorrhages. The blood within its cavities does not clot readily. The fetus of an eclamptic mother may show identical lesions in its organs.

These are the main findings noted at autopsy. Summarized, they consist of multiple thrombosis throughout the organs, which, when combined with focal necrosis in the liver, and multiple hemorrhages, justify the post mortem diagnosis of eclampsia.

Acute yellow atrophy of the liver in over 60 per cent occurs during pregnancy. It is a rare disorder marked by profound toxemia, prostration, jaundice and coma. The liver first enlarges and then rapidly atrophies. Leucin and tyrosin may be recovered from the urine. The liver early shows fatty degeneration and later shrinking and atrophy. Central necrosis of the lobules in the early stages, complete destruction of many lobules in the later stages characterize the process. The writer reported a case which recovered (73).

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CHAPTER XIV

MALFORMATIONS

Malformations of the genital tract may occur together with malformations of the entire individual or may be found in otherwise normal beings.

The experimental work of Stoddard (1) tends to show that *monstra in defectu* and *monstra in excessu* are closely similar and can result from the same causes exerted at different periods of development. In his experiments, Stoddard, by changing the temperature or the amount of oxygen available, inhibited the rate of development. "The type of deformity resulting depended upon the developmental moment at which the interruption occurred." The development and growth of individual organs, in the single individual, are interrelated in a way similar to the interrelations between the components of a double specimen.

Mall (2) likewise lays stress upon the effect of nutritional derangement due to slight lesions of the chorion. From this cause monsters and malformations may arise.

The formations to be discussed include those of excess, as a third ovary, and those of defect, for example, absence of the ovary from or lack of formation or from aplastic degeneration of the anlage. Failure of union of the double müllerian system accounts for double uteri and vaginae and failure of regression of the male portion of the bisexual system (wolffian system) produces various types of hermaphroditism.

Most malformations occur prenatally, only a few develop postnatally, as for instance, the uterus infantilis.

As Ballantyne (3) justly says, "Genital deformities generally represent early stages in development which have failed to pass on into later and more mature phases."

The formation of the female genital system was summarily dealt with in Chapter IV (p. 70). Figs. 59–65, p. 67 *et seq.*, show the müllerian system from which fallopian tubes, uterus and vagina are formed, and the wolffian structures, which, in both the male and female, supply the gonad (formed from the mesonephric ridge and germinal epithelium), and in the female the vestigial epoöphoron and paroöphoron. For details see Felix (4).

The vulva is formed from the ectoderm or skin structures.

The hymen has been described as partly of ectodermal, partly of müllerian formation (bilamellate) or of purely vaginal derivation (Taussig, 5). The complex relations resulting from the coalescence of the uro-

genital sinus, müllerian and wolffian systems and the vulva, readily account for the numerous malformations noted at the vaginal outlet.

In 600 autopsies performed on females, v. Winckel (6) found, in 2 per cent, malformations of the sexual organs. If minor defects, especially post natal deficiencies such as infantilism, are included, the percentage rises (see p. 508).

EXCESS FORMATIONS

Ovary.—*Supernumerary* or *third ovaries* are rare. Such organs must have either a third tube or utero-ovarian ligament. In v. Winckel's case

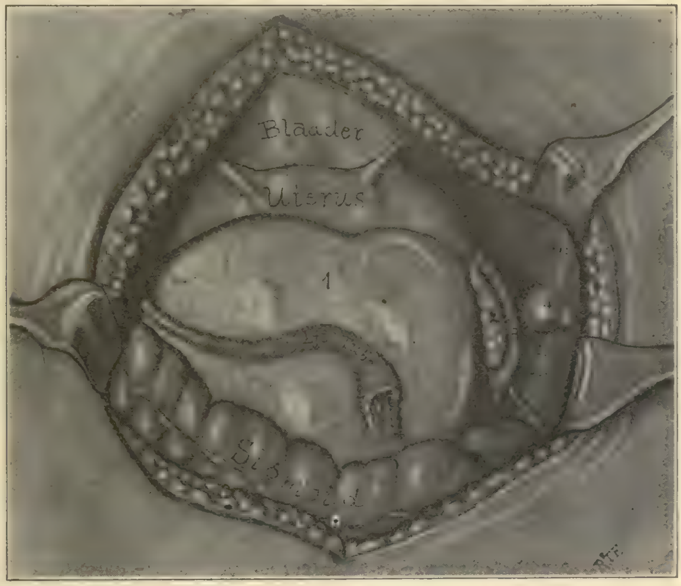

FIG. 331.—PAPILLARY CYSTADENOMA OF A SUPERNUMERARY OR THIRD OVARY. 1. Intraligamentous cyst of the left ovary over which the much elongated tube is drawn out. 2. Normal right ovary. 3. Normal right tube. 4. Supernumerary ovary and tube, situated over the right external iliac artery.

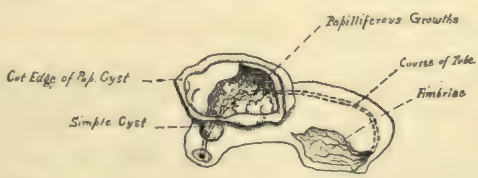

FIG. 332.—DISSECTION OF THE THIRD OVARY AND TUBE SEEN IN FIG. 331. Shows cystic ovary, and pervious tube with fimbrial end closed off.

the ovary lay in the uterovesical pouch; in the writer's case (7) the ovary was situated over the external iliac artery (Figs. 331 and 332).

Accessory ovaries commonly occur as small pedunculated masses attached to the main part of the gland (see Fig. 256, p. 368), or as detached

particles found on the posterior abdominal wall along which the "descent" of the ovary takes place, in Douglas' cul-de-sac, etc. Mauclaire and Eisenberg-Paperin (8) reported 50 cases.

Both types of excess ovarian formation are of interest because they may account for the continuation of menstruation after double oöphorectomy and may be the seat of ovarian tumors.

Bilobed ovaries and other minor changes in the ovary are acquired (see p. 367).

Tube.—Accessory ostia, either sessile or pedunculated, accessory tubes with or without a lumen, in some cases leading into the main tube and forming communicating passages, in others mere diverticula, are frequent (4 to 10 per cent, Ballantyne, l. c. 3). Such appendages are said to give rise to cystic formations (see p. 349). Huffman (9) described a tube which was double-barreled in its ampullary portion. Third tubes are rare and occur in conjunction with supernumerary ovaries (7).

Ectopic gestation may be due in some instances to an ovum arrested in an accessory tube (see p. 445). Impregnation has taken place by way of an accessory ostium, the normal ostia of both tubes having been found closed.

Uterus.—Ballentyne (3) cites three cases of an accessory uterus occurring as an appendage (either anterior or lateral) to an otherwise normal uterus.

A trifid uterus was reported by Depage (see l. c. 3) consisting of a uterus bicornis unicollis to the cervix of which was attached a rudimentary lobe, consisting of a closed sac containing blood.

Vagina.—True excess is reported in only two instances accounted for by duplication due to fusion of two rudimentary individuals. In Gemmell and Paterson's case (10) there were two widely separated uteri, two vaginae, two vulvae, two urinary bladders, but only one anal opening. The woman had been pregnant in each uterus. Both in this case and in the similar case of a child reported by Suppiger (see l. c. 3) the lower part of the spinal column was duplicated.

Vulva.—True duplication occurred in the two cases just described under vagina. Otherwise the condition is limited to united female twins with two pelves.

The clitoris may be hypertrophic; a masculine characteristic noted in pseudohermaphrodites or in combination with hermaphroditism (see p. 500). Such hyperplasia may also occur in response to adrenal overactivity. Hyperplasia of the labia minora (Hottentot apron) is uncommon.

DEFECTS AND RUDIMENTARY FORMATIONS

Ovary.—Bilateral absence probably occurs only in non-viable monsters, although Menge (11) accepts the case of Morgagni in which an otherwise symmetrical but hypoplastic genital apparatus existed.

Unilateral absence may be combined with absence of one Müller's duct (absent tube, uterus unicornis), absence of the kidney of the affected side, or the rest of the genital apparatus may be normal.

The missing ovary may have been twisted off during fetal or adult life, in which case part of the tube usually is also lacking (see p. 368).

Tube.—Bilateral absence of the tube is rare and usually accompanies absence of the uterus. Unilateral defects may be complete or occur in any portion of the length of the oviduct. Portions of the tube may remain solid (without lumen), or in hypoplastic condition, the epithelial lining being devoid of cilia (Hoehne, 12).

Spencer (13) describes the tubes reduced to mere button-like rudiments attached to the uterine cornua. The ovaries were enclosed in peritoneal pouches containing vestigial fimbriae.

Rudimentary tubes commonly occur where the uterus also is rudimentary. Corkscrewlike convolutions in otherwise normal oviducts are a sign of infantilism (see Chapter XV, p. 508).

Uterus.—Bilateral absence of uterus and vagina (for the deficiency of the müllerian duct usually affects the entire lower portions running in the genital cord (see Fig. 333)) occurs only in non-viable monsters. Extreme aplasia producing rudimentary uterus and vagina is uncommon. Complete unilateral agnesia produces a real uterus unicornis (*vide infra*). For details see under "Failure of Fusion of Müller's Ducts" (p. 494), because the various combinations of non-union and defective development are often coincident malformations and are best discussed together.

Vagina.—Vaginal defect so often accompanies uterine deficiency that it will be well to discuss it in that connection. With uterus unicornis a narrow, somewhat laterally situated vagina may be formed from the lower end of one müllerian tube.

Atresias will be discussed in a separate paragraph.

Vulva.—Absence of the vulva is noted only in non-viable monsters. Beneath the skin, which is devoid also of an anal opening, may be a cloaca receiving the urinary, genital and intestinal canals, or a urogenital sinus with separate rectum.

Anus vulvalis (atresia ani vaginalis) in which the anus is absent, the rectum opening into the vulva behind the hymen, results from incomplete separation due to partial nondescent of the rectovaginal septum. Perineal and rectovaginal openings have been described.

Atresia vulvae superficialis consist of agglutination of the labia (see Vulva, p. 105).

Infantile vulva may persist in adult life. The vulva is symmetrical but small. Absence of clitoris or labia is very uncommon. Rarely the perineum has failed to form, the unduly long vulva and the normally situated anus then communicating.

Epispadias consists of fission or defective formation of the anterior wall of the urethra. In extreme degrees it is often combined with separa-

tion of the pubic bones and defective formation of the anterior abdominal and bladder walls (ectopia vesicae). The clitoris is cleft.

Hypospadias is a deficiency of the lower or posterior wall of the urethra due to incomplete development of the urethrovaginal septum. The urogenital sinus persists as a funnel-shaped opening in place of the scaphoid vestibule, the urethra ending higher up in the contracted vagina. In extreme degrees (very rare), the entire posterior urethral wall is lacking.

Congenital Displacements and Malpositions.—These diseases of the genital tract have been sufficiently discussed under the various organs.

The ovaries and tubes may be found in inguinal and other herniae (see pages 329 and 369). The uterus, too, especially if bifid, may form the contents of a hernia (see p. 176). Congenital prolapse together with spina bifida has been referred to (p. 173). Uterine retroversion and retroflexion may be congenital and often is combined with hypoplasia of the sacro-uterine ligaments. Gross displacements of the vagina and vulva are almost unknown. R. Meyer (14) has described a clitoris situated on the perineum.

MALFORMATIONS OF THE UTERUS AND VAGINA RESULTING FROM FAILURE OF FUSION OF THE MÜLLERIAN DUCTS, ETC.

Müller's ducts, in the early embryo appear as cornet-shaped funnels, the ostia abdominales, which grow vertically downward, by means of budlike projections, lateral to the wolffian ducts until they reach the point of insertion of the inguinal folds (later the round ligaments) (see Fig. 333). The ducts then bend sharply inward until they touch in the middle line, make another right angle bend and run downward parallel to each other and to the wolffian ducts, forming the so-called genital cord, or uterovaginal anlage. At their lower end the ducts again make a sharp bend forward, producing the short horizontal limbs which break into the urogenital sinus. The mesenchyme supplies the musculature covering the epithelial tubes and thus gives to the uterus its external form.

First a fusion of the two contiguous mesial walls of Müller's ducts occurs to form a single septum. Later this septum is absorbed in a caudocranial direction, thus producing the single uterovaginal canal. Above the uterine insertion of the round ligaments the ducts throughout life remain unfused as the fallopian tubes.

The complex processes which go to form the uterus and vagina, of which the barest outline is given above, sufficiently account for the frequent disturbances in development and the resulting malformations. Nonunion of the ducts throughout their entirety or in segments, rudimentary development of parts, failure to become excavated, result in diverse malformations which v. Winckel (l. c. 6) has rubricated under 37 forms. Simpler classi-

fications suffice for general use—Kaufmann's schema (15) slightly amplified, appears adequate.

1. **Malformations Due to Faulty Juxtaposition of Müller's Ducts** (uterine portions of tubes, according to Felix (l. c., 4, p. 932) (Fig. 334, a–d)).—*a.* Uterus Didelphys (Fig. 334, a) (uterus duplex separatus).—Complete separation of bodies and cervices; very rare. Two separate vaginae exist.

b. Uterus Duplex Bicornis (Fig. 334, b).—A common variety. The cervices are joined. The vagina may be double, septate (above or below) or single. The one horn may be rudimentary, either solid or excavated.

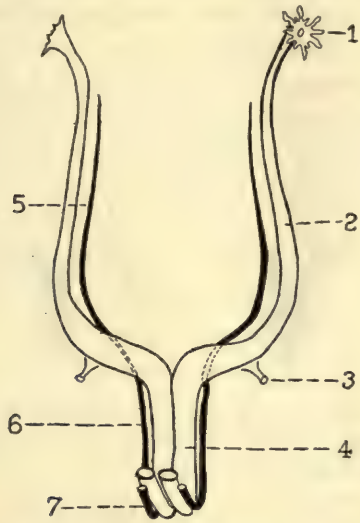

Fig. 333.—Diagram showing the course of Müller's and the wolffian ducts in the human embryo. (Wolffian system in solid black.) 1. Ostium abdominale tubae. 2. Tubal portion of Müller's duct. 3. Inguinal fold (round ligament). 4. Lower vertical part of Müller's duct running in the genital cord (formed by the two müllerian and wolffian ducts). 5. Upper part of wolffian duct. 6. Lower vertical part of wolffian duct. 7. Lower horizontal part of wolffian duct.

In this and in the preceding type a broad peritoneal band may run from rectum to bladder (rectovesical ligament). It occurs in about 10 per cent of cases. Etiologically it can have no significance in causing the malformation. Advanced grades of uterus bicornis are often wrongly called uterus didelphys. They may be named uterus pseudodidelphys.

c. Uterus Bicornis Unicollis.—A bifid corpus with a single cervix and single vagina (Fig. 334, c).

In both 1 (a and b) and 2 (a) twin pregnancies are unduly frequent, as 1 to 12 instead of as 1 to 90 (Jellinghaus, 16). Dystocia due to the septa is common. Pregnancy may take place in a rudimentary horn. Such a pregnancy acts much like a tubal pregnancy, most usually ending in

rupture in the later months (see p. 452). A rudimentary atretic excavated horn (Fig. 336, b) may menstruate and become the site of an hematometra.

d. UTERUS BICORNIS SEPTUS.—Septum throughout the length of the uterus. Externally a mere depression in the fundus.

FIG. 334.—DIAGRAM OF MALFORMATIONS DUE TO FAULTY JUXTAPOSITION OF MÜLLER'S DUCTS. *a.* Uterus didelphys. *b.* Uterus bicornis duplex (pseudo-didelphys). *c.* Uterus bicornis unicollis. *e.* Uterus arcuatus.

UTERUS ARCUATUS (Fig. 334, d).—The external fundal concavity is the sole evidence of bicornate malformation.

2. **Malformations Due to Faulty Absorption of Septa** (Fig. 335, a–d). *a.* UTERUS SEPTUS DUPLEX CUM VAGINA SEPTA (uterus bilocularis)

FIG. 335.—DIAGRAM OF MALFORMATIONS DUE TO LACK OF ABSORPTION OF SEPTA. *a.* Uterus septus duplex cum vagina septa. *b.* Uterus septus duplex. *c.* Uterus subseptus. *d.* Uterus biforis supra simplex.

(Fig. 335, a)—Externally appears normal, internally is divided into two halves by an antero posterior partition.

b. UTERUS SEPTUS DUPLEX (Fig. 335, b).—The vagina being single.

c. UTERUS SUBSEPTUS (Fig. 335, c).

d. UTERUS BIFORIS SUPRA SIMPLEX (Fig. 335, d).

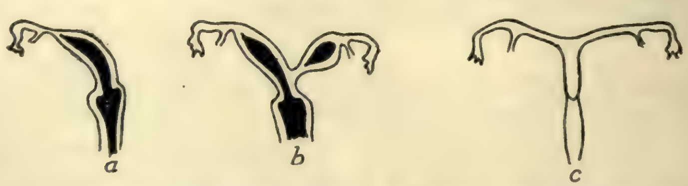

FIG. 336.—MALFORMATIONS DUE TO APLASIA. *a.* Uterus unicornis (one müllerian duct aplastic). *b.* Uterus bicornis cum rudimento cornu alterius partim excavatus. *c.* Uterus rudimentarius solidus.

3. **Malformations Due to Aplasia (absence).**—*a.* Complete absence of tubes, uterus and vagina (see p. 493). *b.* Complete absence of one müllerian tube (uterus unicornis) (Fig. 336, a). *c.* Symmetrical absence of parts, as of uterine body, cervix, vagina or parts of vagina.

4. Malformations Due to Hypoplasia (rudimentary development).—*a*. Symmetrical, as uterus rudimentarius solidus (Fig. 336, c). *b*. Asymmetrical, as uterus bicornis cum rudimento cornu alterius (excavatus sive solidus) (Fig. 336, b). Very frequent form. Such a rudimentary horn may form a beadlike, solid mass, a strand, or hollow elongated tube at the side of the better developed uterus. The communicating stalk may be solid or hollow. The round ligament inserts into the horn. Pregnancy or hematocolpos may develop when there is a lumen. *c*. Fetal uterus shows persistence in the adult as the small uterus with long cervix and cervical rugae extending to the fundus, which is normal in fetal life. *d*. Infantile uterus, see p. 508.

Malformations and Pregnancy.—Most of the effects are largely of clinical interest, including the frequency of twins, frequency of abortion, of different degrees of development of the twins, possibility of long interval (weeks or months) between the expulsion of the fetuses in different halves, the frequency of transverse (43 per cent) and breech positions, of undue frequency of tears in septa and uterus, of post-partum hemorrhage from non-contractility of septa when the placenta is inserted on the dividing wall. Abortion or dystocia may arise from incarceration of the pregnant half in a hernia or in the pelvis.

In the non-pregnant, completely separated, or partly fused half and in the excavated atretic horn, a decidua forms during pregnancy. Observations of menstruation from the non-pregnant half are all of old date. Usually from three to five days post partum the decidua is expelled.

Various accidents, such as bursting of the uterine wall during pregnancy and rupture of the uterine body or cervix during labor, depend partly on the poverty in muscle and elastic elements. The transverse position of a fetus with head in one cavity of a uterus bicornis septus, the feet in the other horn, is a purely mechanical effect, as is the dystocia due to vaginal septa. The placenta may be on one side of a septate uterus, the fetus in the other. For details and literature see E. Wertheim in v. Winckel's Handbuch der Geburtshilfe 2, i, p. 391, Wiesbaden, 1904.

ATRESIAS

The fallopian tubes, usually in conjunction with the rest of the müllerian tract, may be solid or only partly excavated. Excavated rudimentary horns with imperforate connecting stalk represent a form of uterine atresia (Fig. 336, b). Rarely congenital atresia at the external or internal os uteri has been reported. Usually such stenoses are acquired (see p. 179).

The commonest atresias are vulvar and vaginal. According to Chrobak and Rosthorn (17) all atresias are uncommon, occurring only in 0.04 per cent of gynecological cases.

Vulvar Agglutination.—This has been discussed on p. 105 and p. 493. Most often the disease is acquired in late fetal or early postnatal life.

Hymenal closures may be developmental or acquired. If acquired the hymen may prove unduly thick. The imperforate hymen in both varieties is lined externally with stratified squamous epithelium, and internally with the same or with a single layer of cylindrical epithelium.

Vaginal Atresias.—*a.* In extreme forms the entire vagina is represented by a fibrous or fibromuscular cord situated between bladder and rectum. Usually the uterus is maldeveloped, often a uterus bipartitus solidus (Küstner, 18). The vulva may be normal or abnormal, the hymen absent or well-developed. Horseshoe kidney in the plevis or over the sacrum has been found (Brettauer, 19). Male pseudohermaphrodites with cryptorchid testes may be mistaken for a female with vaginal atresia.

b. Other types of vaginal atresias vary from transverse, complete or incomplete *septa* to long, solid areas without lumen. The favorite sites are the junction of the lower and upper with the middle third. Superimposed multiple septa are unusual. Veit and others far too dogmatically, ascribe ail atresias, not accompanied by other malformations, to acquired inflammatory causes (see p. 138).

The septa may be retrohymenal, close to and adherent to the cervix, or in intermediate locations. The septa may be membranous or thick and fleshy. Perforate septa, according to Brickner (20), occur about once in 5000 patients and are atavistic remains, being normally found in the chimpanzee, sheep, dugong, etc. According to Ballantyne (l. c. 3, p. 271) Vautrin found such a perforated septum in a lateral atretic vagina.

c. Atresia of a lateral vagina results when one half of a double vagina is imperforate. The cavity may communicate above with a cervix of a double uterus, or end blindly. Blood may accumulate in its lumen.

Retention of Mucus and Blood Consequent to Atresias.—Before puberty, especially in the newborn, large quantities of mucus may be found behind an imperforate hymen, and may produce an abdominal tumor (Vitrac, see Chrobak and Rosthorn, l. c. 17, p. 198).

After menstruation has been established, each period is characterized by an increasing accumulation of blood behind the point of atresia. More than 3½ liters of chocolate-colored, tarry fluid have been found.

The fluid is usually devoid of fibrin ferment and is sterile. The red blood cells may be laked, appearing as blood shadows. Infection may occur from the blood stream, from the intestine by continuity, or result from aspiration (pyocolposmetra, etc.).

The tumor resulting from the accumulation of blood is called hematocolpos, hematometra, hematosalpinx or hematovarium, depending upon the cavity or organ in which it collects. At the onset some hypertrophy of the walls of the canal occurs above the site of the atresia, later atrophy with marked thinning of the walls takes place.

The epithelial lining of the genital canal regularly persists, though thin-

ning and atrophy of the cells may be noted, especially in the vagina. The tubal wall may become paper thin.

Brothers (20), in 164 cases of blood retention, found 145 of primary origin. Of these 80 occurred in simple, undivided genitals, 65 in genitals duplicated somewhere in their course. Hematovarium occurred 16 times.

Almost any division of the genital canal may be distended. Most often the vagina is filled, the uterus riding upon the vaginal sac like a small knob.

The tubes are not always involved. According to Veit, infection must exist before the abdominal ostium can be closed and distention take place. The theory does not hold good in every case, extrusion of aseptic blood sufficing to produce peritubal adhesions and ostial closure. Sudden emptying of the blood tumor from below may rupture the hematosalpinx and cause peritonitis (see p. 328).

Spontaneous perforation of the blood tumor into bladder, rectum or through the occluding septum often occurred before the operative era.

For tumors situated in malformed genitals consult Melson (p. 285).

HERMAPHRODITISM

Much deadwood has accumulated in the literature dealing with the subject of hermaphroditism. In what follows only such facts as are of immediate interest and importance will be discussed.

Physiological hermaphroditism occurs among plants in which self-fecundation may take place. Among some of the lower animals the male gland functionates first and the testis becomes inactive when the ovary, in turn, assumes its function. *Accidental* hermaphroditism only, is found among vertebrates. In such cases the gonad of one sex usually predominates, the other sex gland being rudimentary. For details see Pick (22) and Lacassagne (23). Hermaphroditism presupposes the presence of the sex glands characteristic of both sexes. To postulate functional activity of both components is unnecessary, especially in the male sex, in which the male characters are surely bound to the interstitial cells and not to the spermatozoids. This is evident in cryptorchid testes in which spermatogenesis is regularly defective.

Hermaphroditism Verus.—This form is rare. The gonads of both sexes must be represented either as separate glands (testis and ovary) or as compound glands (ovotestis). The attributes of one or the other sex usually predominate. The degree of maleness or femaleness is a purely quantitative attribute as is evident from the experiments of Riddle on birds and of Steinach on mammals.

Lacassagne (l. c. 23) has catalogued the cases reported as true hermaphrodites. Only a few will bear strict critique. Among these the most striking are the following:

Salen's case had a right ovotestis and a left ovary. The female characters predominated (female habitus, vagina, menstruation).

Sinagaglia's case showed no external malformations except that the right

testicle was not in the scrotum. This cryptorchid gland was removed and found to be an ovotestis in close connection with a tube and atrophic uterus and a vas deferens. The testicular portion showed seminiferous tubules in the infantile stage, the ovarian part contained primordial follicles and corpora fibrosa. The semen contained spermatozoa, therefore the second testis must have been functionating.

Lacassagne (with Brian and Lagoutte) published the case of a supposed male 28 years of age. The left sex gland lay in the pelvis in close apposition to tube and ovary, the right one lay at the external inguinal ring in the position of a testis. The left ovotestis contained follicles and a corpus luteum, and a testicular portion developed to the spermatogonia stage. The right, seemingly a testicle, contained male elements, including spermatocytes, well-developed interstitial cells and female gametes in the form of primordial follicles.

Tubular Hermaphroditism (synonymous with male or female internal pseudohermaphroditism).—This is a normal condition in every human embryo during the time in which both the müllerian (later forming tube, uterus and vagina) and wolffian ducts (later forming rete testis, vas deferens and prostate) coexist. During normal development, the organs of the opposite sex involute and, in the female, remain as paroöphoron, epoöphoron and Gärtner's duct.

When prostate and vas deferens are found, but the sex glands are female, the hermaphroditism is female tubular. In a male, vagina, uterus and tubes more or less well developed may be found in addition to testes, seminal vesicles and vasa deferentia.

External Pseudohermaphroditism (external pseudohermaphroditism masculinus or femininus).—This may or may not be combined with internal, either tubular or true hermaphroditism. In itself it consists merely in malformation of the external genitalia.

In the female these most commonly include hypertrophic clitoris, defective vagina and united labia with, in some cases, labial hernia of the ovary. In the male a hypoplastic phallus, cleft scrotum, cryptorchism and hypospadias simulate a vulva. A more or less developed urogenital sinus may persist, forming a funnel-shaped rudimentary vagina. According to Felix (l. c. 4, p. 964), scrotal hypospadias is a development of the sinus urogenitalis in the female sense.

Inversion of all the secondary sex characters, accentuation of a single one such as hirsutism, or nondevelopment of all the characteristics of sex (neuter stage) add to the confusion.

Neugebauer (24) has described tumors occurring in the genitals of pseudohermaphrodites. These include carcinoma, sarcoma, dermoids and teratomata. See also Pick (l. c. 22).

It has become more and more evident that histological examination of the gonad is the sole sure criterion in determining the sex of hermaphroditic individuals.

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CHAPTER XV

THE GLANDS OF INTERNAL SECRETION IN GYNECOLOGY AND OBSTETRICS

Our knowledge of the endocrine glands is as yet incomplete. There is no reason, however, why the ordinary rules of common sense and good judgment should not be applied to "endocrinology" just as to other branches of medicine. The present tendency to ascribe all obscure conditions to derangement of the glands of internal secretion is as unwarranted as the tendency to overestimate the therapeutic value of endocrine preparations. A continuation of this tendency will inevitably result in throwing the practice of "endocrinology" into the hands of quacks and fakirs.

For general literature on the glands of internal secretion see Biedel, Vincent, Falta (1).

The organs of internal secretion can be divided into those essential to life, these are the hypophysis or pituitary, the parathyroids, the pancreas and the adrenals, and those whose removal is survived, which are the epiphysis or pineal, the thyroid, the thymus (if this be an endocrine organ), and the gonads (ovary and testis). Each of these organs is anatomically characterized by definite cellular structure (for details of which see books on histology). Correspondingly, each of the glands exerts characteristic functions. Whether one gland can vicariously functionate in place of another is an open question.

Many of the glands are compound in nature, for example, the pancreas. Through the duct of Wirsung this gland excretes enzymes into the lumen of the duodenum; its internal secretory function is carried on by the Islands of Langerhans whose secretion, as is that of all the other endocrine glands, is carried off by the blood stream. Such dual nature is characteristic of the testis, in which the semen is the external and the interstitial cells are the internal secretory factors, and the ovary, in which the ova represent the external secretion, the corpus luteum the endocrine part.

A different type of compound gland is the pituitary, the anterior lobe of which is glandular in nature and essential to life. The posterior lobe secretes a simple substance, "pituitrin," which acts upon the blood pressure. The thyroid-parathyroid complex may also be regarded as dual, the parathyroids being essential elements for the continuance of life, fatal tetany resulting from complete parathyroidectomy. If the thyroid is ablated, life continues, though marked impairment of metabolism results. Finally the suprarenal complex consists of two distinct components, the lipoidal cortex and the pigmented chromaffin medulla. Both of these appear essential to life, although the presence of other chromaffin areas, throughout the abdominal ganglia, makes ablation of the medulla inconclusive, as these small accessory bodies act vicariously.

The secretion of endocrine organs are called *hormones.* Such as have been isolated, are comparatively simple chemical substances. The simplest hormonelike body, resulting from tissue oxidation and therefore not the product of a gland, is carbon dioxide, which carried in the blood stream, acts upon the blood pressure and respiratory centers. The hormones, which have been isolated, are adrenalin, pituitrin and thyroxin. Of these only the last mentioned can fully replace the action of the gland from which it is derived. The others are only partial and incomplete substitutes and are in every way comparable to drugs which act upon the musculature and involuntary nervous system.

The glands of internal secretion produce definite compounds, each one characteristic of the gland by which it is elaborated. Consequently in response to functional demands (normal or abnormal stimuli) the cells may produce too much secretion, or if exhausted or diseased, may produce too little secretion. It is as impossible, from the viewpoint of the writer, to conceive that the peptic cells of the stomach can produce trypsin as that the endocrine cells can produce a changed secretion. In other words, the conception of "dysfunction" should be dropped, "hyper" and "hypo" function alone being retained.

Our knowledge of the function of the various endocrine glands was first obtained by observation of disease followed by autopsy control. Thus Addison's and Graves' disease and acromegaly were observed. Next came experimental investigation based mainly upon complete or partial ablation of one or more glands. Lately substitution by means of organ extracts has been essayed. By these means considerable insight into the function of the individual glands has been obtained.

In studying the function of the endocrine organs attention must be paid to their effect at different periods of existence.

1. *In fetal life* the pancreas is active and can help a pancreatectomized mother to continue to exist. Carlson (2) removed the pancreas of a pregnant bitch, who continued to live much longer than a non-pregnant animal could have done. From this he concludes that the pancreas of the fetuses functionated for the mother. Adrenalin is found in very small fetuses. The other glands have not as yet been sufficiently studied.

2. *Immediately after birth,* and continuing for a period of one to three weeks, the uterus of the newborn is enlarged and turgid. In a moderate number of instances a sanguineous discharge appears at the vulva. The breasts of both male and female infants may be enlarged and contain colostrum. Halban (3) has shown that these phenomena are due to the maternal placenta. During intra-uterine life the placenta produces growth and hyperplasia of the fetal uterus and breast. After birth when the inhibition exerted by the placenta is withdrawn, uterine bleeding and mammary secretion result.

3. *During infancy* the effect of the endocrine organs on the sexual tract in health appears to be imperceptible. A number of instances of precocious

maturity evidenced by appearance of menstruation, growth of pubic hair, development of breasts and larger body size in childhood have been described (Lenz, Harris, 4). In some cases no recognizable disease was found; in others tumors of the ovary, pineal or adrenal glands were causative as proved by regression of the precocious sex phenomena after removal of the growth (Harris, l. c. 4). The mentality of these children remains infantile, even if their body size and sex equipment approaches that of puberty.

The symptoms described are apparently due to diverse causes. The pineal tumors are usually teratomata and have been interpreted as producing either hyper- or hypofunction of the gland (?). The ovarian growths almost always produce hyperfunction. The adrenal cortical growths are also interpreted as productive of excess action.

Ablation of any of the glands by experimental means, or hypofunction produced by pathological conditions occurring before puberty, cause a different effect than if the same conditions occur after maturity has been reached.

Hypopituitarism in childhood produces dwarfism; *hypothyroidism* produces cretinism, *hypo-ovarian function* results in infantilism of the genitals and secondary sex characters, *hypopinealism* causes precocious sex development.

Hyperfunction produces equally characteristic changes.

Hyperpituitarism in infancy causes gigantism, *hyperthymism* may produce status thymo-lymphaticus, *hyperadrenalism* is followed by precocious puberty with excess of male sex characters (in utero it may produce feminine pseudohermaphroditism), *hyperovarian* development may produce similar symptoms.

4. *After puberty* and full growth has been attained the effects of endocrine disturbances are somewhat different. Schematicized, they may be represented as follows:

	Hyperfunction	Hypofunction	Extracts	Ablation Effects
Hypophysis	Acromegaly	Dystrophia adiposo genitalis	Ant. lobe prolongs life after hypophysectomy: Post. lobe elevates blood pressure	Ant. lobe cachexia and death: Post. lobe, diabetes insipidus
Pineal	Obesity (?)	Unknown	(?)	Negative
Thyroid	Exophthalmic goitre	Myxedema	Thyroxin fully replaces gland	Cachexia strumipriva
Parathyroid	Unknown	Tetany	Ameliorate tetany symptoms	Fatal tetany
Thymus	Unknown	Unknown	(?)	None
Pancreas	Unknown	Diabetes	Ineffective	Diabetes, cachexia, death
Ovaries	Menorrhagia	Amenorrhea: Sterility	Results very doubtful	Artificial menopause
Testis	(?)	Impotence	Ineffective	Impotence
Adrenal	Hypertrichosis	Addison's disease	Adrenalin: Increase of blood pressure	Glycosuria, weakness, death

The effect of the endocrine glands upon metabolism is but partially understood. The thyroid, the chromaffin system and the posterior lobe of the pituitary stimulate and increase metabolic activity. The anterior lobe

of the pituitary, the pancreas and parathyroids, according to Falta (l. c. 1), decrease it.

Of all the endocrine glands the thyroid most directly effects the body metabolism. Consequent to removal of the entire thyroid gland the metabolism is reduced to 30 per cent of the normal. What mechanism keeps the function at this minimum level is not known (Kendall). Thyroxin quantitatively increases the metabolic rate.

Fig. 337.

Fig. 338.

Fig. 337.—Female, twenty-three years old. Eunuchoid type but with predominatingly female secondary sex characters. Height 6 ft. 1 in.; limbs long, larnyx small, voice high pitched. Breasts, pelvis and hair distribution feminine.

Fig. 338.—A typical hypopituitary syndrome. Girl, sixteen years, height 5 ft. 9 in.; weight 241 lbs., diffuse hair on face, never menstruated. genitals infantile, increased carbohydrate tolerance.

According to Loewy and Richter (5), oxidation is reduced after removal of the ovaries. Murlin and Bailey (6) also found a reduction of from 6 to 17 per cent but do not ascribe the effect directly to action of the ovary.

Bone growth is influenced by the anterior lobe of the pituitary. Indirectly the gonads influence this factor, ablation producing long eunchoid types, early maturation resulting in short, stocky individuals.

Nervous equilibrium is maintained by a balance between excitant (or stimulative) and inhibitory factors. This automatic and subconscious control applies to involuntary muscle (including heart muscle, unstriped muscle of blood vessels, intestine, uterus, etc.) and to glands. It is exerted through the autonomic nervous system.

The autonomic system consists of a reflex mechanism composed of an efferent or motor arc which receives impulses originating reflexly and involuntarily in the cord, or perhaps also in the higher centers. The impulses are transmitted through two neurons. The first consist of cells in the central nervous system which send medullated axis cylinders outward through the mid brain, medulla and spinal cord (preganglionic fibers). A connection (synapse) with an extra-spinal ganglion carries the impulse to the destined spot (postganglionic fibers).

In the midbrain the preganglionic fibers accompany the third, seventh, ninth, tenth and eleventh nerve (craniobulbar). In the cord from the second dorsal to the third lumbar these fibers appear as the anterior roots (cervico-thoracico lumbar autonomic or "sympathetic") and end in the cervical (stellate, inferior and superior cervical), abdominal (coeliac, inferior and superior mesenteric, renal, aortic, etc.) and pelvic ganglia.

The postganglionic fibers pass back to the spinal nerves and traveling in the nerves, reach the muscle or gland which they control. For details see Jackson (7).

The ovaries or testes function as organs of internal secretion even after their nerve supply has been severed, as shown by transplantation. The thyroid, pituitary and adrenal are influenced by nerve control. Hyperactivity of these three glands produces excessive sympathetic excitation (Jackson, l. c. 7).

Depending upon whether the cervico-thoracico-lumbar (sympathicotonia) or the craniobulbosacral (vagotonia) division shows hyperirritability, certain symptoms develop. The main manifestations, according to Jackson, are as follows:

Cranio-bulbo-sacral
Hyperactivity = Vagotonia
3d N. Myosis
  Accommodation spasm
5 and 7 N. Salivation
10 N. Bronchial asthma
  Bradycardia (relieved by atropine)
Sacral. Increased tone of bladder wall
General: Eosinophilia
  Increased fat and carbohydrate tolerance
  Dermographia.

Cervico-thoracico-lumbar
Hyperactivity = Sympathicotonia
Cervical, Mydriasis
  Exophthalmos
  Dryness of mouth
Thoracico Lumbar
  Tachycardia
Lumbar
  Relaxed bladder
  Eosinopenia
  Decreased fat and carbohydrate tolerance.

Balance of these antagonistic nervous systems is largely maintained through hormonic action, imbalance may be due to hormonic disturbance. The so-called artificial menopause symptoms (flushes, sweats, nervous irritability) commonly seen after double oöphorectomy, are striking examples of this imbalance.

Sensitiveness to pilocarpine (0.01 gm.) evidenced by cardio-respiratory arrhythmia, and increases in carbohydrate tolerance bespeaks vagotonia, according to many authors.

Sensitiveness to adrenalin, 0.5 to 1.0 milligram, signifies sympathicotonia. A rise of 15 or more millimeters in blood pressure (Hg), development of palpitation and tremors, and a decrease in carbohydrate tolerance is regarded as a positive reaction.

As the causes of either vagus or sympathetic preponderance are most varied (vagus hyperactivity or sympathetic hypo-activity, thyroid hyperactivity, etc., etc.), the symptoms vary, and responses to drug reactions likewise vary and become misleading. *The same individual may be hypersensitive* to both varieties of drugs.

The foregoing has given a rapid survey of the functions of the various endocrine organs, their relation to the body complex and to each other. The function of the ovary in relation to the generative tract in health has been fully discussed in Chapter IV, p. 80.

Because of dearth of material, and of lack of exact observation, it is still necessary to describe derangements of the endocrine glands largely in terms of function instead of in terms of pathological changes. Frequently, too, no recognizable changes can be found. This applies especially to the ovary.

Do disturbances of ovarian function produce disturbances in the genital tract and in the entire organism?

Disturbances of Ovarian Function—Hypofunction.—It is almost impossible to dissociate the ovarian function completely from that of other endocrine glands. *Castration,* which is the most extreme manifestation of hypofunction, in infancy produces a eunuchoid type characterized by long, slender body, neuter or male pelvis, atrophic external and internal genitals and infantile secondary sex characters, which include scant hair, undeveloped breasts, lack of subcutaneous fat. Castration in adults causes amenorrhea, rapid atrophy of external and especially of internal genitals and manifestations of the artificial menopause (vide ante). For details see Frank (8).

Castration causes the anterior lobe of the pituitary to increase. Its eosinophile cells become more numerous. The changes in other glands are less marked.

Minor degrees of hypofunction produce amenorrhea or reduced and irregular menstruation. Temporary or permanent sterility may result (as in lactation atrophy).

Severer forms of hypoövarism may accompany general subnormality, status lymphaticus and infantilism. The uterus is infantile (see below),

the tubes convoluted, the ovaries large (Herrmann, Chrobak and Rosthorn, 9).

Infantilism.—The affected individual remains more or less infantile in body, psychic and sex equipment. Sometimes gross endocrine lesions such as dwarfism or myxedema exist; more often general hypoplasia, anemia or chlorosis, congenital syphilis or bad heredity can be noted.

The stature is usually slight, the bones light, the lower extremities short, the spine flat, the pelvis narrow and generally contracted with narrow subsymphesial angle and high promontory. The chin is receding, the teeth far apart and their enamel defective, the hard palate high and arched. Hypoplasia of the heart and aorta are often present.

The secondary sex characters are poorly developed or neuter. The hair is scant, often the lanugo remains, the mons is poorly covered. The breasts are small, the nipples retracted. The larynx remains high and small.

The vulva is funnel-shaped, the labia small, the perineum poorly developed. The vagina is narrow, the fornices small, the portio conical but short. The uterus is short, narrow, flabby. The cervix is long compared to the ill-developed corpus. Douglas's cul-de-sac descends deeply as in the fetus. The tubes retain their fetal corkscrew windings. The ovaries are small and elongated and may be situated in the kidney region.

The bladder may be extrapelvic, narrow and retain the fetal spindle shape. The appendix vermiformis may be wide at its base, as in animals.

In keeping with these physical findings the infantile individual is commonly mentally subnormal, shows poor resistance to disease and to the wear and tear of life, is sexually frigid, sterile and amenorrheic. In minor grades the various systems may be affected in different degrees, for example the sexual organs may suffer most.

For details see Chrobak and Rosthorn (9).

These authors found infantilism present in 3 per cent of 2500 cases. Others have reported as high as 25 per cent in their gynecological cases.

Hyperfunction as seen in infancy may cause premature sex development. In adult life hyperfunction may be hard to analyze, as complicating factors, such as inflammation of the genital organs, may obscure the issue.

Probably quantitative increase in corpus luteum secretion, when long continued, will produce the hyperplastic mucosa and thick fibrotic muscle described under "fibrosis uteri," (p. 194). Pelvic congestion, menorrhagia and metrorrhagia are noted, but these two symptoms may occur as well where no anatomical changes can be found. These troubles are most frequent at the period of puberty and the preclimacterium. It is also not unlikely that uterine fibroids (fibromyoma) are due to ovarian hyperactivity.

A transient period of hyperovarian function is the rule in the early stages of hyperthyroidism and hyperpituitarism. This overexcitation is regularly followed by a hypoövarian state. In debilitating constitutional

diseases (chlorosis, tuberculosis, nephritis, etc.) a hypoövarian condition almost always ultimately results.

The exciting factor may be distant, as for instance in the hypophysis, but in every case the direct influence no matter whether hyper- or hypofunctional, is exerted by excitation or inhibition of the ovary. Whether the follicle secretion, the corpus luteum secretion or the interstitial cells exert different effects is still unsettled.

The effect of *ovarian extracts* is problematical. Their therapeutic application is at present purely empirical. To transfer the results obtained by the writer (10) in animals to human beings would require a daily dosage of 4 grams of active corpus luteum extract to be given to a 75 kg. female in hypodermic form. For an entertaining and just critique of the explorers, pathfinders, pirates and camp followers in the, as yet unexplored, field of "endocrinology," the reader is referred to Cushing's article (11).

In pregnancy the evidence in regard to ovarian function is conflicting (l. c. 8) and obscured by the effect of the placenta (Frank, 12). Hypophyseal hyperactivity is shown by increase in the size of the pituitary, increase in its chromophobe cells and recurrent acromegalic symptoms in succeeding pregnancies (Marek, 13). Adrenal hyperfunction not infrequently causes hypertrichosis (Jellinghaus, 14), pigmentation and cholesterinemia, due to changes in the adrenals (Kolde, 15). Thyroid enlargement is noted in 65 to 90 per cent, and absence of this hyperplasia produces symptoms (Ward, 16).

No proof exists that *eclampsia* is due to endocrine disturbance (see Frank, 17). The improvement or cure of *osteomalacia* by double oöphorectomy (Seitz, 18) bespeaks the possibility of ovarian hyperfunction.

Tetany is largely a pregnancy disease. Probably greater demands are made upon the detoxicating function of the parathyroids during gestation.

Addison's disease (adrenal hypofunction) regularly produces sterility. Only in four cases did pregnancy occur.

To summarize, it may be said that in order to produce a perfect individual and maintain perfect health the interaction of the glands of internal secretion must be normal. Disturbance of this perfect interrelation reacts upon the genital sphere in one of two ways—in an increase or a decrease of function. Genital hypofunction manifests itself locally by aplasia of the genitals, systemically by the signs of infantilism, eunuchoidism and other variations dependent not only upon the time of onset but also upon the degree of involvement of other ductless glands. Genital hyperfunction manifests itself by locally well-developed genitals (even in infancy), or by uterine hyperplasia ("metritic" uterus, fibroids ?). Systemically, except in infancy as shown by premature sexual ripening, no changes are noted unless some of the other glands are simultaneously affected.

A symposium dealing with the entire subject, as presented at the meeting of the American Gynecological Society in 1917, will be found in the Sep-

tember number of Surgery, Gynecology and Obstetrics, 1917, XXV, pp. 225–360.

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